Supplementary file 3: GRADE, Certainty of Evidence, Summary of Findings Tables and Evidence-to-Decision Frameworks

Children (2-<12y)

QUESTION

Should nutrition interventions vs. treated/untreated comparators be used for weight maintenance/loss in children experiencing overweight or obesity?	
POPULATION:	Children living with overweight or obesity
INTERVENTION:	Nutrition interventions (dietary approaches with no specific daily energy intake goal) vs untreated comparator (baseline to final end-point)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also	

had higher mortality from coronary heart disease and stroke in adulthood (9).

Blood glucose level
Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6).

Type 2 diabetes mellitus
Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10).

Non-alcoholic fatty liver disease
Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14).

Musculoskeletal conditions
Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15).

Cancer
Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19).

Mental health
Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22).

Health-related quality of life ratings
Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23).

	Reproductive health Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Dietary approaches with no specific daily energy intake goal ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from meta-analyses: From 1 study (25) with 52 intervention participants and 49 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.32 lower (95% CI 0.71 lower to 0.07 higher) in the nutrition (dietary approaches with no specific daily energy intake goal) intervention versus an untreated comparator. Additional desirable effects: No evidence was identified in this population. Lived experience: Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (26, 27). Reductions in mental health symptoms including depression and anxiety (28, 29), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (28) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (30, 31). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (30, 32-34). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (30). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (30, 33, 35-37). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (30, 33, 38).	The benefits of weight loss or maintenance on cardiometabolic outcomes in children were also considered by the Guidelines Development Committee when making a judgement. Research findings from multiple, large community-based longitudinal studies (e.g., Healthy Communities Study (39), Healthy China Initiative (40), the Physical Activity and Nutrition in Children Study (41)) overwhelmingly support positive health outcomes of improved nutrition.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Dietary approaches with no specific daily energy intake goal ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from meta-analyses: No evidence was identified in this population. Additional undesirable effects: No additional undesirable effects were identified Lived experience: Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty	In addition to intentional adiposity loss, some children living with overweight or obesity may experience a slowing down of bone accretion.

	managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (30, 33, 36). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (30, 32, 33). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (31, 36, 42). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (33, 38).	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Dietary approaches with no specific daily energy intake goal ● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. The evidence is very uncertain about the effect of dietary approaches with no specific daily energy intake goal on adiposity in this population group.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of the child patient and their caregivers in relation to receiving nutrition interventions. However, the committee believes that since there are benefits, most children with overweight or obesity and their caregivers would opt for this treatment.	Some children living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Dietary approaches with no specific daily energy intake goal ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

intervention ○ Varies ○ Don't know		

Resources required

How large are the resource requirements (costs)?"

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Nutrition interventions are not widely available, and many are not affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention	No evidence on the cost effectiveness of this intervention was identified for this population.	

○ Varies ● No included studies		

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving nutrition treatments. However, the committee believes this intervention is likely to be acceptable to the majority of children with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where nutrition is individually tailored and culturally and/or linguistically appropriate. Interventions should be appropriate for the developmental stage of the child. The mental health of the child should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not systematically collected scientific evidence regarding feasibility of nutrition interventions.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Dietary approaches with no specific daily energy intake goal may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083

21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Hao M, Han W, Yamauchi T. Short-term and long-term effects of a combined intervention of rope skipping and nutrition education for overweight children in Northeast China. Asia Pac J Public Health. 2019;31(4):348-58. doi: 10.1177/1010539519848275
26. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
27. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
28. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
29. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
30. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
31. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
32. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
33. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
34. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
35. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
36. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
37. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
38. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53
39. Strauss WJ, Nagaraja J, Landgraf AJ, Arteaga SS, Fawcett SB, Ritchie LD, et al. The longitudinal relationship between community programmes and policies to prevent childhood obesity and BMI in children: the Healthy Communities Study. Pediatr Obes. 2018;13(S1):82-92. doi: 10.1111/ijpo.12266
40. Chen P, Wang D, Shen H, Yu L, Gao Q, Mao L, et al. Physical activity and health in Chinese children and adolescents: expert consensus statement (2020). Br J Sports Med. 2020;54(22):1321-31. doi: 10.1136/bjsports-2020-102261
41. Lakka TA, Lintu N, Väistö J, Viitasalo A, Sallinen T, Haapala EA, et al. A 2 year physical activity and dietary intervention attenuates the increase in insulin resistance in a general population of children: the PANIC study. Diabetologia. 2020;63(11):2270-81. doi: 10.1007/s00125-020-05250-0
42. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782

Question: Nutrition interventions compared to treated/untreated comparators for weight maintenance/loss in children experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	nutrition interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Nutrition intervention* **vs untreated comparator (baseline to final end-point)** – meta-analysis												
1[a]	randomised trials	very serious[b]	not serious	not serious	serious[c]	none	52	49	-	Hedges' g 0.32 lower (0.71 lower to 0.07 higher)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

*Dietary approaches with no specific daily energy intake goal, CI: confidence interval

Explanations

a. 1 study, with 2 subgroup populations (girls, boys)

b. -2 using RoB-2 risk of bias rated High for all outcomes

c. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)

QUESTION

Should physical activity interventions vs. treated/untreated comparators be used for weight maintenance/loss in children experiencing overweight or obesity?	
POPULATION:	Children living with overweight or obesity
INTERVENTION:	Physical activity interventions (aerobic exercise) vs untreated comparator (baseline to final end-point)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with	

healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6).

<u>Type 2 diabetes mellitus</u>
Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10).

<u>Non-alcoholic fatty liver disease</u>
Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14).

<u>Musculoskeletal conditions</u>
Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15).

<u>Cancer</u>
Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19).

<u>Mental health</u>
Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22).

<u>Health-related quality of life ratings</u>
Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23).

<u>Reproductive health</u>

	Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Aerobic Exercise: ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis:</u> From 1 study (25) with 54 intervention participants and 49 comparator participants, evidence demonstrated a small important effect of Hedges' g 0.3 lower (0.68 lower to 0.09 higher) in the aerobic exercise intervention versus an untreated comparator. <u>Evidence from narrative synthesis:</u> 1 study (26) unable to be included in meta-analysis found a favourable effect of physical activity (aerobic exercise) interventions on weight maintenance/loss in both the sample experiencing overweight and the sample experiencing obesity. <u>Additional desirable effects:</u> No additional evidence from randomised controlled trials or review papers were available for desirable effects in this population for this intervention. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (27, 28). Reductions in mental health symptoms including depression and anxiety (29, 30), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (29) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (31, 32). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (31, 33-35). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (31). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (31, 34, 36-38). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (31, 34, 39).	Research findings from multiple, large community-based longitudinal studies (e.g., Healthy Communities Study (40), Healthy China Initiative (41), the Physical Activity and Nutrition in Children Study (42)) overwhelmingly support positive health outcomes of physical activity. The benefits of weight loss or maintenance on cardiometabolic outcomes in children were also considered when making judgement.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Aerobic Exercise: ● Trivial ○ Small ○ Moderate	<u>Evidence from meta-analysis:</u> No evidence was identified in this population. <u>Additional undesirable effects:</u>	A low risk of incidental musculoskeletal injury exists for children with overweight or obesity during physical

○ Large ○ Varies ○ Don't know	No additional undesirable effects were identified in this population. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (31, 34, 37). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (31, 33, 34). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (32, 37, 43). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (34, 39). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (31, 32, 43).	activity. Strategies that incorporate inclusion, engagement and awareness of weight stigma, and sensitivities are needed, as this is an age when participation rates, particularly among girls, begin to decline.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Aerobic Exercise: ● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from meta-analysis:</u> The evidence is very uncertain about the effect of physical activity (aerobic exercise) on adiposity. <u>Evidence from narrative synthesis</u>: Physical activity (aerobic exercise) likely results in little to no difference in adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of the child patient and their caregivers in relation to receiving physical activity treatment. However, the committee believes that since there are benefits, most children living with overweight or obesity and their caregivers would opt for this treatment.	Some children living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

Aerobic Exercise: ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know	Physical activity interventions are not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options (31, 32, 43). Barriers are exacerbated in rural areas, or areas of low socioeconomic status (39). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing (e.g., team uniforms). Local knowledge is important for increasing accessibility to low-cost physical activity options. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not sourced literature on certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Fees may present financial barriers for participation in extracurricular sporting activities or classes. Equity could be addressed by raising awareness of available treatments and avenues for access among patients and caregivers. For example, highlighting locally available, low-cost physical activity programs, or when discussing the patient's care plan, practitioners should take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or

		inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of children with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where physical activity is individually tailored and culturally and/or linguistically appropriate. Interventions should be appropriate for the developmental stage of the child. The mental health of the child should be considered and monitored
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of physical activity interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	**Varies**	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Aerobic activity interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164

20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Hao M, Han W, Yamauchi T. Short-term and long-term effects of a combined intervention of rope skipping and nutrition education for overweight children in Northeast China. Asia Pac J Public Health. 2019;31(4):348-58. doi: 10.1177/1010539519848275
26. Li Y-P, Hu X-Q, Schouten EG, Liu A-L, Du S-M, Li L-Z, et al. Report on childhood obesity in China (8): effects and sustainability of physical activity intervention on body composition of Chinese youth. Biomed Environ Sci. 2010;23(3):180-7. doi: 10.1016/S0895-3988(10)60050-5
27. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
28. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
29. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
30. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
31. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
32. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
33. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
34. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
35. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
36. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
37. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
38. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
39. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53
40. Strauss WJ, Nagaraja J, Landgraf AJ, Arteaga SS, Fawcett SB, Ritchie LD, et al. The longitudinal relationship between community programmes and policies to prevent childhood obesity and BMI in children: the Healthy Communities Study. Pediatr Obes. 2018;13(S1):82-92. doi: 10.1111/ijpo.12266
41. Chen P, Wang D, Shen H, Yu L, Gao Q, Mao L, et al. Physical activity and health in Chinese children and adolescents: expert consensus statement (2020). Br J Sports Med. 2020;54(22):1321-31. doi: 10.1136/bjsports-2020-102261
42. Lakka TA, Lintu N, Väistö J, Viitasalo A, Sallinen T, Haapala EA, et al. A 2 year physical activity and dietary intervention attenuates the increase in insulin resistance in a general population of children: the PANIC study. Diabetologia. 2020;63(11):2270-81. doi: 10.1007/s00125-020-05250-0

43. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782

Question: Physical activity interventions compared to treated/untreated comparators for weight maintenance/loss in children experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	physical activity interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Physical activity* intervention vs untreated comparator (baseline to final end-point) – Meta analysis												
1[a]	randomised trials	very serious[b]	not serious	not serious	serious[c]	none	54	49	-	Hedges' g 0.3 **lower** (0.68 lower to 0.09 higher)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity
Physical activity intervention vs untreated comparator (baseline to final end-point) – Narrative synthesis												
1[d]	randomised trials	serious[e]	not serious	not serious	not serious	none	1/1 study found a favourable effect of physical activity interventions on weight maintenance/loss in both the population experiencing overweight and the population experiencing obesity.				⨁⨁⨁◯ Moderate	Physical activity likely results in little to no difference in adiposity

*Aerobic exercise intervention, CI: confidence interval

Explanations

a. 1 study, with 2 subgroup populations (girls, boys)
b. -2 using RoB-2 risk of bias rated High for all outcomes
c. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)
d. 1 study, with 2 subgroup populations (experiencing overweight, experiencing obesity)
e. -1 using RoB-2 risk of bias rated Some concerns for all outcomes

QUESTION

Should interventions combining nutrition and physical activity with or without sedentary behaviour intervention vs. treated/untreated comparators be used for weight maintenance/loss in children experiencing overweight or obesity?	
POPULATION:	Children living with overweight or obesity
INTERVENTION:	Combined nutrition and physical activity interventions, with or without sedentary behaviour interventions: • Combined nutrition and physical activity interventions vs untreated comparator (baseline to final end-point). No sedentary behaviour interventions were identified.
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o No o Probably no o Probably yes ● Yes o Varies o Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9).	

	<u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23).	

<table>
<tr><td></td><td><u>Reproductive health</u>
Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).</td><td></td></tr>
<tr><td colspan="3">Desirable Effects
How substantial are the desirable anticipated effects?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>○ Trivial
○ Small
● Moderate
○ Large
○ Varies
○ Don't know</td><td><u>Evidence from meta-analysis</u>:
From 1 study (25) with 48 intervention participants and 49 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.47 lower (0.87 lower to 0.07 lower) in the combined nutrition and physical activity interventions versus an untreated comparator.

<u>Additional desirable effects:</u>
No evidence was identified in this population.

<u>Lived experience:</u>
Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (26, 27). Reductions in mental health symptoms including depression and anxiety (28, 29), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (28) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (30, 31). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (30, 32-34). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (30). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (30, 33, 35-37). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (30, 33, 38).</td><td>Research findings from multiple, large community-based longitudinal studies (e.g., Healthy Communities Study (39), Healthy China Initiative (40), the Physical Activity and Nutrition in Children Study (41)) overwhelmingly support positive health outcomes of improved nutrition and physical activity.

The benefits of weight loss or maintenance on cardiometabolic outcomes in children were also considered when making judgement.</td></tr>
<tr><td colspan="3">Undesirable Effects
How substantial are the undesirable anticipated effects?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>○ Trivial
○ Small
○ Moderate
○ Large
○ Varies
● Don't know</td><td><u>Evidence from the narrative synthesis</u>:
2 studies (42, 43) unable to be included in the meta-analysis found a combined nutrition and physical activity intervention may result in little to no difference to adiposity.

<u>Additional undesirable effects:</u>
No additional undesirable effects were identified in this population.

<u>Lived experience:</u>
Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience</td><td>A low risk of incidental musculoskeletal injury exists for children with overweight or obesity during physical activity.

Strategies that incorporate inclusion, engagement and awareness of weight stigma and sensitivities are needed, as this is an age when</td></tr>
</table>

	challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (30, 33, 36). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (30, 32, 33). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (31, 36, 44). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (33, 38). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (30, 31, 44).	participation rates, particularly among girls, begin to decline.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table Evidence from meta-analysis: The evidence is very uncertain about the effect of combined nutrition, and physical activity interventions on adiposity in this population. Evidence from narrative synthesis: A combined nutrition and physical activity intervention may result in little to no difference to adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of the child patient and their caregivers in relation to receiving combined nutrition and physical activity treatment. However, the committee believes that since there are benefits, most children living with overweight or obesity and their caregivers would opt for this treatment.	Some children living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence, and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition and physical activity interventions are not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options (30, 31, 44). Barriers are exacerbated in rural areas, or areas of low socioeconomic status (38). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing (e.g., team uniforms). Local knowledge is important for increasing accessibility to low-cost physical activity options. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate	We have not assessed the certainty of evidence of required resources.	

○ High ● No included studies		

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ No included studies	Of 35 behavioural modification intervention studies included in a scoping review, study authors reported that 30 were cost effective (45). All 13 interventions in school settings, four of six in community settings, and 13 of 16 in hospital settings were cost effective. No summary of the changes in quality-adjusted life years (QALYs) was provided. The heterogeneity of outcome measures used in the studies limited the comparability of results. In a systematic review of economic evaluations of interventions targeting overweight or obesity in childhood, 22 studies of treatment-only interventions (behavioural interventions with diet and physical activity components) for children were identified (46). Of these 22 interventions, study authors reported that 19 were cost effective.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. Fees may present financial barriers for participation in extracurricular sporting activities or classes. Equity could also be addressed by raising awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and

		linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition and physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of children with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where nutrition and physical activity is individually tailored, and culturally and/or linguistically appropriate. Interventions should be appropriate for the developmental stage of the child. The mental health of the child should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition and physical interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Combined nutrition and physical activity interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164

20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Hao M, Han W, Yamauchi T. Short-term and long-term effects of a combined intervention of rope skipping and nutrition education for overweight children in Northeast China. Asia Pac J Public Health. 2019;31(4):348-58. doi: 10.1177/1010539519848275
26. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
27. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
28. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
29. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
30. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
31. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
32. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
33. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
34. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
35. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
36. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
37. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
38. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53
39. Strauss WJ, Nagaraja J, Landgraf AJ, Arteaga SS, Fawcett SB, Ritchie LD, et al. The longitudinal relationship between community programmes and policies to prevent childhood obesity and BMI in children: the Healthy Communities Study. Pediatr Obes. 2018;13(S1):82-92. doi: 10.1111/ijpo.12266
40. Chen P, Wang D, Shen H, Yu L, Gao Q, Mao L, et al. Physical activity and health in Chinese children and adolescents: expert consensus statement (2020). Br J Sports Med. 2020;54(22):1321-31. doi: 10.1136/bjsports-2020-102261
41. Lakka TA, Lintu N, Väistö J, Viitasalo A, Sallinen T, Haapala EA, et al. A 2 year physical activity and dietary intervention attenuates the increase in insulin resistance in a general population of children: the PANIC study. Diabetologia. 2020;63(11):2270-81. doi: 10.1007/s00125-020-05250-0
42. Li Y-P, Hu X-Q, Schouten EG, Liu A-L, Du S-M, Li L-Z, et al. Report on childhood obesity in China (8): effects and sustainability of physical activity intervention on body composition of Chinese youth. Biomed Environ Sci. 2010;23(3):180-7. doi: 10.1016/S0895-3988(10)60050-5

43. Williams CF, Bustamante EE, Waller JL, Davis CL. Exercise effects on quality of life, mood, and self-worth in overweight children: the SMART randomized controlled trial. Transl Behav Med. 2019;9(3):451-9. doi: 10.1093/tbm/ibz015
44. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782
45. Dhillon A, Mayer M, Kysh L, Fox DS, Hegedus E, Vidmar AP. Cost-effectiveness analysis of individual-level obesity treatment in paediatrics: A scoping review. Pediatr Obes. 2024;19(3):e13100. doi: 10.1111/ijpo.13100
46. Onyimadu O, Violato M, Astbury NM, Hüls H, Heath L, Shipley A, et al. A systematic review of economic evaluations of interventions targeting childhood overweight and obesity. Obes Rev. 2023;24(9):e13597. doi: 10.1111/obr.13597

Question: Interventions combining nutrition and physical activity with or without sedentary behaviour compared to treated/untreated comparators for weight maintenance/loss in children experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interventions **combining nutrition and physical activity** with or without **sedentary behaviour**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Combined nutrition and, **physical activity interventions* vs untreated comparator (baseline to final end-point)** – Meta-**analysis**												
1[a]	randomised trials	very serious[b]	not serious	not serious	serious[c]	none	48	49	-	Hedges' g **0.47 lower** (0.87 lower to 0.07 lower)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.
Combined nutrition and **physical activity vs untreated comparator (baseline to final end-point)** – Narrative synthesis												
3[d]	randomised trials	serious[e]	serious[f]	not serious	not serious	none	1/3 studies found a positive effect of combining nutrition and physical activity interventions for weight maintenance/loss; 2/3 studies found a negative effect of combining nutrition and physical activity interventions for weight maintenance/loss				⨁⨁◯◯ Low	Combined nutrition and physical activity interventions may result in little to no difference in adiposity

*No interventions with sedentary behaviour were identified, CI: confidence interval

Explanations

a. 1 study, with 2 subpopulations (girls, boys)
b. -2 using RoB-2 risk of bias rated High for all outcomes
c. -1 Imprecision due to small sample size (Total n<400)
d. 3 studies, with 3 intervention arms
e. -1 using RoB-2 risk of bias rated Some concerns (2 (67%) outcomes), High (1 (33%) outcome)
f. -1 due to unspecified heterogeneity due to differences in exposure

QUESTION

Should interventions combining nutrition, physical activity, and psychological interventions vs. treated/untreated comparators be used for weight maintenance/loss in children experiencing overweight or obesity?	
POPULATION:	Children living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and psychological interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u>	

	Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23). <u>Reproductive health</u>	

	Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from narrative synthesis:</u> 1 study unable to be included in a meta-analysis favoured the intervention for weight maintenance/loss. BMI z-score-for-age decreased by 0.07 in the intervention arm and increased by 0.03 in the control arm (25). <u>Additional desirable effects:</u> No additional evidence from randomised controlled trials or review papers were available for desirable effects in this population for this intervention. <u>Lived experience</u>: Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (26, 27). Reductions in mental health symptoms including depression and anxiety (28, 29), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (28) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (30, 31). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (30, 32-34). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (30). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (30, 33, 35-37). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (30, 33, 38).	Current available data indicates a reduction in eating disorder symptoms (binge eating) with weight management treatments that combine nutrition, physical activity, and psychological approaches. Research findings from multiple, large community-based longitudinal studies (e.g., Healthy Communities Study (39), Healthy China Initiative (40), the Physical Activity and Nutrition in Children Study (41)) overwhelmingly support positive health outcomes of improved nutrition and physical activity. The benefits of weight loss or maintenance on cardiometabolic outcomes in children were also considered when making judgement.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analysis:</u> No evidence was identified in this population. <u>Additional undesirable effects</u>: No evidence was identified in this population. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as	A low risk of incidental musculoskeletal injury exists for children with overweight or obesity during physical activity. Strategies that incorporate inclusion, engagement and awareness of weight stigma and sensitivities are needed, as this is an age when participation rates,

	over-exercising were identified (30, 33, 36). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (30, 32, 33). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (31, 36, 42). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (33, 38). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (30, 31, 42).	particularly among girls, begin to decline.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from narrative synthesis:</u> The evidence is very uncertain about the effect of combined nutrition, physical activity, and psychological interventions on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of the child patient and their caregivers in relation to receiving combined nutrition, physical activity, and psychological treatment. However, the committee believes that since there are benefits, most children living with overweight or obesity and their caregivers would opt for this treatment.	Some children living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention	Research evidence was drawn from desirable and undesirable effects, certainty of evidence, and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

o Varies o Don't know		

Resources required
How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition, physical activity, and psychological interventions are not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options (30, 31, 42). Barriers are exacerbated in rural areas, or areas of low socioeconomic status (38). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing (e.g., team uniforms). This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited, particularly access to psychological treatments. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness
Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours	No evidence on the cost effectiveness of this intervention was identified for this population.	

the intervention ○ Favours the intervention ○ Varies ● No included studies		

Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Equity is affected by cost of treatments and accessibility of treatments. Food security and cost of living affect equity: Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. Fees may present financial barriers for participation in extracurricular sporting activities or classes. High cost of psychological care and long wait times may make treatment prohibitive, decreasing health equity. Equity could also be addressed by raising awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with

		overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition, physical activity, and psychological treatments. However, the committee believes this intervention is likely to be acceptable to the majority of children with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where nutrition, physical activity and psychological treatment are individually tailored and culturally and/or linguistically appropriate. Interventions should be appropriate for the developmental stage of the child. The mental health of the child should be considered and monitored.

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition, physical activity, and psychological interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Combined nutrition, physical activity, and psychological interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164

20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Guo H, Zeng X, Zhuang Q, Zheng Y, Chen S. Intervention of childhood and adolescents obesity in Shantou city. Obes Res Clin Pract. 2015;9(4):357-64. doi: 10.1016/j.orcp.2014.11.006
26. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
27. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
28. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
29. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
30. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
31. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
32. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
33. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
34. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
35. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
36. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
37. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
38. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53
39. Strauss WJ, Nagaraja J, Landgraf AJ, Arteaga SS, Fawcett SB, Ritchie LD, et al. The longitudinal relationship between community programmes and policies to prevent childhood obesity and BMI in children: the Healthy Communities Study. Pediatr Obes. 2018;13(S1):82-92. doi: 10.1111/ijpo.12266
40. Chen P, Wang D, Shen H, Yu L, Gao Q, Mao L, et al. Physical activity and health in Chinese children and adolescents: expert consensus statement (2020). Br J Sports Med. 2020;54(22):1321-31. doi: 10.1136/bjsports-2020-102261
41. Lakka TA, Lintu N, Väistö J, Viitasalo A, Sallinen T, Haapala EA, et al. A 2 year physical activity and dietary intervention attenuates the increase in insulin resistance in a general population of children: the PANIC study. Diabetologia. 2020;63(11):2270-81. doi: 10.1007/s00125-020-05250-0
42. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782

Question: Interventions combining nutrition, physical activity, and psychological compared to treated/untreated comparators for weight maintenance/loss in children experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interventions combining nutrition, physical activity and psychological	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Combined nutrition, physical activity and psychological interventions vs untreated comparator (baseline to 12 months)												
1[a]	randomised trials	very serious[b]	not serious	not serious	very serious[c]	none	1/1 study favoured the intervention for weight maintenance/loss. BMI z-score-for-age decreased by 0.07 in the intervention arm and increased by 0.03 in the control arm.				⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 1 study, with 1 intervention arm

b. -2 using RoB-2 risk of bias rated High (1 (100% outcome)

c. -2 Imprecision due to very small size (Total n<50)

QUESTION

Should interventions combining nutrition, physical activity, and family-centred interventions vs. treated/untreated comparators be used for weight maintenance or loss in children experiencing overweight or obesity?	
POPULATION:	Children living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and family-centred interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u>	

	Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23). <u>Reproductive health</u>	

	Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis:</u> From 8 studies (25-32) with 677 intervention participants and 605 comparator participants, evidence demonstrated a small important effect of Hedges' 0.15 lower (95% CI 0.3 lower to 0.00 higher) in the nutrition, physical activity, and family-centred interventions versus comparator. <u>Evidence from narrative synthesis:</u> 1 study (33) unable to be included in a meta-analysis found a positive effect of combining nutrition, physical activity, and family-centred interventions on weight maintenance/loss. The proportion of participants who were defined as living with overweight or obesity increased by 3.06% in the intervention arm compared to an increase of 5.88% in the comparator arm. <u>Additional desirable effects</u>: No evidence was identified in this population. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (34, 35). Reductions in mental health symptoms including depression and anxiety (36, 37), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (36) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (38, 39). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (38, 40-42). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (38). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (38, 41, 43-45). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (38, 41, 46).	The benefits of weight loss or maintenance on cardiometabolic outcomes in children were also considered when making judgement. Research findings from multiple, large community-based longitudinal studies (e.g., Healthy Communities Study (47), Healthy China Initiative (48), the Physical Activity and Nutrition in Children Study (49)) overwhelmingly support positive health outcomes of improved nutrition and physical activity.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

<table>
<tr><td>● Trivial
○ Small
○ Moderate
○ Large
○ Varies
○ Don't know</td><td>Evidence from meta-analyses:
No evidence was identified in this population.

Additional undesirable effects:
No additional undesirable effects were identified in this population.

Lived experience:
Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (38, 41, 44). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (38, 40, 41). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (39, 44, 50). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (41, 46). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (38, 39, 50).</td><td>A low risk of incidental musculoskeletal injury exists for children with overweight or obesity during physical activity.

Strategies that incorporate inclusion, engagement and awareness of weight stigma and sensitivities are needed, as this is an age when participation rates, particularly among girls, begin to decline.</td></tr>
<tr><td colspan="3">Certainty of evidence
What is the overall certainty of the evidence of effects?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>● Very low
○ Low
○ Moderate
○ High
○ No included studies</td><td>Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table.

Evidence from meta-analysis:
The evidence is very uncertain about the effect of combined nutrition, physical activity, and family-centred interventions on adiposity.

Evidence from narrative synthesis:
Combined nutrition, physical activity, and family-centred interventions may attenuate an increase in adiposity.</td><td></td></tr>
<tr><td colspan="3">Values
Is there important uncertainty about or variability in how much people value the main outcomes?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
● Probably no important uncertainty or variability
○ No important uncertainty or variability</td><td>We have not sourced literature on the preferences and values of child patients and their caregivers in relation to receiving combined nutrition, physical activity, and family-centred treatment. However, the committee believes that since there are benefits, most children living with overweight or obesity and their caregivers would opt for this treatment.</td><td>Some children living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.</td></tr>
<tr><td colspan="3">Balance of effects
Does the balance between desirable and undesirable effects favour the intervention or the comparison?</td></tr>
</table>

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence, and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition, physical activity, and family-centred interventions are not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options (38, 39, 50). Barriers are exacerbated in rural areas, or areas of low socioeconomic status (46). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing (e.g., team uniforms). This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ● Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	The findings of a systematic review were that family-based behavioural interventions were not cost effective for targeting obesity in children, or produced better outcomes at higher costs than comparators (51).	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity: Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. Fees may present financial barriers for participation in extracurricular sporting activities or classes. Equity could also be addressed by raising awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas,

		having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Family-based weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition, physical activity, and family-centred interventions. However, the committee believes this intervention is likely to be acceptable to the majority of children with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where nutrition, physical activity and family-centred interventions are individually tailored and culturally and/or linguistically appropriate. Interventions should be appropriate for the developmental stage of the child. The mental health of the child should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition, physical activity, and family-centred interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	**Probably favours the comparison**	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Combined nutrition, physical activity and family-centred interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3

19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Crespo NC, Talavera GA, Campbell NR, Shadron LM, Behar AI, Slymen D, et al. A randomized controlled trial to prevent obesity among Latino paediatric patients. Pediatr Obes. 2018;13(11):697-704. doi: 10.1111/ijpo.12466
26. Gerards SMPL, Dagnelie PC, Gubbels JS, van Buuren S, Hamers FJM, Jansen MWJ, et al. The effectiveness of lifestyle triple P in the Netherlands: a randomized controlled trial. PLoS ONE. 2015;10(4):e0122240. doi: 10.1371/journal.pone.0122240
27. Gong L, Yuan F, Teng J, Li X, Zheng S, Lin L, et al. Weight loss, inflammatory markers, and improvements of iron status in overweight and obese children. J Pediatr. 2014;164(4):795-800.e2. doi: 10.1016/j.jpeds.2013.12.004
28. Siegrist M, Lammel C, Haller B, Christle J, Halle M. Effects of a physical education program on physical activity, fitness, and health in children: the JuvenTUM project. Scand J Med Sci Sports. 2013;23(3):323-30. doi: 10.1111/j.1600-0838.2011.01387.x
29. Smith JD, Berkel C, Carroll AJ, Fu E, Grimm KJ, Mauricio AM, et al. Health behaviour outcomes of a family based intervention for paediatric obesity in primary care: a randomized type II hybrid effectiveness-implementation trial. Pediatr Obes. 2021;16(9):e12780. doi: 10.1111/ijpo.12780
30. Wake M, Lycett K, Clifford SA, Sabin MA, Gunn J, Gibbons K, et al. Shared care obesity management in 3-10 year old children: 12 month outcomes of HopSCOTCH randomised trial. BMJ. 2013;346:f3092. doi: 10.1136/bmj.f3092
31. Waling M, Lind T, Hernell O, Larsson C. A one-year intervention has modest effects on energy and macronutrient intakes of overweight and obese Swedish children. J Nutr. 2010;140(10):1793-8. doi: 10.3945/jn.110.125435
32. Derwig M, Tiberg I, Björk J, Kristensson Hallström I. Changes in perceived parental self-efficacy after a Child-Centred Health Dialogue about preventing obesity. Acta Paediatr. 2022;111(10):1956-65. doi: 10.1111/apa.16453
33. Davis SM, Myers OB, Cruz TH, Morshed AB, Canaca GF, Keane PC, O'Donald ER. CHILE: outcomes of a group randomized controlled trial of an intervention to prevent obesity in preschool Hispanic and American Indian children. Prev Med. 2016;89:162-8. doi: 10.1016/j.ypmed.2016.05.018
34. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
35. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
36. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
37. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
38. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
39. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
40. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
41. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771

42. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
43. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
44. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
45. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
46. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53
47. Strauss WJ, Nagaraja J, Landgraf AJ, Arteaga SS, Fawcett SB, Ritchie LD, et al. The longitudinal relationship between community programmes and policies to prevent childhood obesity and BMI in children: the Healthy Communities Study. Pediatr Obes. 2018;13(S1):82-92. doi: 10.1111/ijpo.12266
48. Chen P, Wang D, Shen H, Yu L, Gao Q, Mao L, et al. Physical activity and health in Chinese children and adolescents: expert consensus statement (2020). Br J Sports Med. 2020;54(22):1321-31. doi: 10.1136/bjsports-2020-102261
49. Lakka TA, Lintu N, Väistö J, Viitasalo A, Sallinen T, Haapala EA, et al. A 2 year physical activity and dietary intervention attenuates the increase in insulin resistance in a general population of children: the PANIC study. Diabetologia. 2020;63(11):2270-81. doi: 10.1007/s00125-020-05250-0
50. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782
51. Sampaio F, Nystrand C, Feldman I, Mihalopoulos C. Evidence for investing in parenting interventions aiming to improve child health: a systematic review of economic evaluations. Eur Child Adolesc Psychiatry. 2024;33(2):323-55. doi: 10.1007/s00787-022-01969-w

Question: Interventions combining nutrition, physical activity and family-centred compared to treated/untreated comparators for weight maintenance/loss in children experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	interventions **combining nutrition, physical activity and family-centred**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Combined nutrition, physical activity and family-centred interventions vs untreated comparator (baseline to 12 months) - meta-**analysis**												
8[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	677	605	-	Hedges' g **0.15 lower** (0.3 lower to 0.00 higher)	⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.
Combined nutrition, physical activity and family-centred interventions vs untreated comparator (baseline to 12 months) - narrative synthesis												
1[e]	randomised trials	serious[f]	not serious	not serious	serious[g]	none	1/1 study found a positive effect of combining nutrition, physical activity and family-centred interventions on weight maintenance/loss. The proportion of participants who were defined as living with overweight or obesity increased by 3.06% in the intervention arm compared to an increase of 5.88% in the comparator arm.				⊕⊕◯◯ Low	Combined nutrition, physical activity and family-centred interventions may attenuate an increase adiposity.

CI: confidence interval

Explanations

a. 8 studies, with 8 intervention arms
b. -1 using RoB-2 risk of bias rated Low (4 (18%) outcomes), Some concerns (15 (68%) outcomes), High (3 (14%) outcomes)
c. -1 Inconsistency of I^2=51.28%
d. -1 Imprecision due to 95% CI crosses 1
e. 1 study, with 1 intervention arm
f. -1 using RoB-2 risk of bias rate Some concerns for all outcomes
g. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should a combination of nutrition and family-centred interventions vs. treated/untreated comparators be used for weight maintenance/loss in children experiencing overweight or obesity?	
POPULATION:	Children living with overweight or obesity
INTERVENTION:	Combined nutrition and family-centred interventions: • Nutrition and family-centred interventions versus any comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with	

	healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated	

	that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from narrative synthesis:</u> 4 studies unable to be included in a meta-analysis favoured combining nutrition and family-centred interventions for weight maintenance/loss compared to comparator (25-28). <u>Additional desirable effects</u>: No evidence was identified in this population. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (29, 30). Reductions in mental health symptoms including depression and anxiety (31, 32), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (31) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (33, 34). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (33, 35-37). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (33). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (33, 36, 38-40). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (33, 36, 41).	The benefits of weight loss or maintenance on cardiometabolic outcomes in children were also considered when making judgement. Research findings from multiple, large community-based longitudinal studies (e.g., Healthy Communities Study (42), Healthy China Initiative (43), the Physical Activity and Nutrition in Children Study (44)) overwhelmingly support positive health outcomes of improved nutrition.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analysis:</u> No data <u>Additional undesirable effects:</u> No additional undesirable effects were identified in this population. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (33, 36, 39). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural	In addition to intentional adiposity loss, some children living with overweight or obesity may experience a slowing down of bone accretion.

	changes caused conflict over necessary behavioural adjustments (33, 35, 36). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (34, 39, 45). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (36, 41). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (33, 34, 45).	

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table Nutrition and family-centred interventions may reduce adiposity.	

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of child patients and their caregivers in relation to receiving combined nutrition and family-centred treatment. However, the committee believes that since there are benefits, most children living with overweight or obesity and their caregivers would opt for this treatment.	Some children living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects
Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

Resources required
How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition and family-centred interventions are not necessarily widely available and affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations.

● Varies ○ Don't know		Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition and family-centred treatments. However, the committee believes this intervention is likely to be acceptable to the majority of children living with overweight or obesity, their parents/caregivers and clinicians.	Acceptability increases where nutrition and family-centred interventions are individually tailored and culturally and/or linguistically appropriate. Interventions should be appropriate for the developmental stage of the child. The mental health of the child should be considered and monitored.

Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition and family-centred interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Combined nutrition and family-centred interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3

19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Díaz RG, Esparza-Romero J, Moya-Camarena SY, Robles-Sardín AE, Valencia ME. Lifestyle intervention in primary care settings improves obesity parameters among Mexican youth. J Am Diet Assoc. 2010;110(2):285-90. doi: 10.1016/j.jada.2009.10.042
26. Okely AD, Collins CE, Morgan PJ, Jones RA, Warren JM, Cliff DP, et al. Multi-site randomized controlled trial of a child-centered physical activity program, a parent-centered dietary-modification program, or both in overweight children: the HIKCUPS study. J Pediatr. 2010;157(3):388-94.e1. doi: 10.1016/j.jpeds.2010.03.028
27. Raynor HA, Osterholt KM, Hart CN, Jelalian E, Vivier P, Wing RR. Efficacy of US paediatric obesity primary care guidelines: two randomized trials. Pediatr Obes. 2012;7(1):28-38. doi: 10.1111/j.2047-6310.2011.00005.x
28. Stettler N, Wrotniak BH, Hill DL, Kumanyika SK, Xanthopoulos MS, Nihtianova S, et al. Prevention of excess weight gain in paediatric primary care: beverages only or multiple lifestyle factors. The Smart Step Study, a cluster-randomized clinical trial. Pediatr Obes. 2015;10(4):267-74. doi: 10.1111/ijpo.260
29. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
30. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
31. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
32. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
33. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
34. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
35. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
36. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
37. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
38. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
39. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
40. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
41. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53

42. Strauss WJ, Nagaraja J, Landgraf AJ, Arteaga SS, Fawcett SB, Ritchie LD, et al. The longitudinal relationship between community programmes and policies to prevent childhood obesity and BMI in children: the Healthy Communities Study. Pediatr Obes. 2018;13(S1):82-92. doi: 10.1111/ijpo.12266
43. Chen P, Wang D, Shen H, Yu L, Gao Q, Mao L, et al. Physical activity and health in Chinese children and adolescents: expert consensus statement (2020). Br J Sports Med. 2020;54(22):1321-31. doi: 10.1136/bjsports-2020-102261
44. Lakka TA, Lintu N, Väistö J, Viitasalo A, Sallinen T, Haapala EA, et al. A 2 year physical activity and dietary intervention attenuates the increase in insulin resistance in a general population of children: the PANIC study. Diabetologia. 2020;63(11):2270-81. doi: 10.1007/s00125-020-05250-0
45. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782

Question: A combination of nutrition and family-centred interventions compared to treated/untreated comparators for weight maintenance/loss in children experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	Inconsistency	Indirectness	Imprecision	Other considerations			
Combined nutrition and family-centred interventions versus any comparator (baseline to 12 months)									
4[a]	randomised trials	serious[b]	serious[c]	not serious	not serious	none	4/4 studies favoured combining nutrition and family-centred interventions for weight maintenance/loss compared to comparator.	⨁⨁◯◯ Low	Combined nutrition and family-centred interventions may reduce adiposity.

CI: confidence interval

Explanations

a. 4 studies, with 5 intervention arms
b. -1 using RoB-2 risk of bias rated Low (1 (25%) study), Some concerns (2 (50%) studies), High (1 (25%) study)
c. -1 due to unspecified heterogeneity due to differences in exposure

QUESTION

Should a combination of four or more behavioural interventions vs. treated/untreated comparators be used for weight maintenance/loss in children experiencing overweight or obesity?	
POPULATION:	Children living with overweight or obesity
INTERVENTION:	Combination of four or more interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with	

	healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated	

	that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis</u>: From 10 studies with 1341 intervention participants and 1047 comparator participants, evidence demonstrated a small unimportant effect of Hedges' g 0.13 lower (95% CI 0.22 lower to 0.05 lower) in the intervention versus comparator (25-34). <u>Evidence from narrative synthesis</u>: 4 intervention arms from 4 additional studies unable to be included in the meta-analysis found a positive effect of combining four or more behavioural interventions on weight maintenance/loss, 1 intervention arm from 1 study showed mixed effects (35-38). <u>Additional desirable effects</u>: No evidence was identified in this population. <u>Lived experience</u>: Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (39, 40). Reductions in mental health symptoms including depression and anxiety (41, 42), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (41) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (43, 44). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (43, 45-47). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (43). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (43, 46, 48-50). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (43, 46, 51).	Less is known about the effects of multimodal approaches to weight management, due in part to the variability in the multiple treatment types, study heterogeneity and low availability of evidence. However, some patients may be encouraged to take up multimodal treatments with specific tailoring to their needs. Research findings from multiple, large community-based longitudinal studies (e.g., Healthy Communities Study (52), Healthy China Initiative (53), the Physical Activity and Nutrition in Children Study (54)) overwhelmingly support positive health outcomes of improved nutrition and physical activity.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analysis</u>: No evidence was identified in this population. <u>Additional undesirable effects</u>: No additional undesirable effects were identified in this population. <u>Lived experience</u>:	A low risk of incidental musculoskeletal injury exists for children with overweight or obesity during physical activity. Strategies that incorporate inclusion, engagement and

<table>
<tr><td></td><td>Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (43, 46, 49). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (43, 45, 46). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (44, 49, 55). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (46, 51). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (43, 44, 55).</td><td>awareness of weight stigma and sensitivities are needed, as this is an age when participation rates, particularly among girls, begin to decline.</td></tr>
<tr><td colspan="3">Certainty of evidence
What is the overall certainty of the evidence of effects?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>○ Very low
● Low
○ Moderate
○ High
○ No included studies</td><td>Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table.

<u>Evidence from both meta-analysis and narrative synthesis:</u>
A combination of four or more behavioural interventions may result in little to no difference in adiposity.</td><td></td></tr>
<tr><td colspan="3">Values
Is there important uncertainty about or variability in how much people value the main outcomes?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>○ Important uncertainty or variability
○ Possibly important uncertainty or variability
● Probably no important uncertainty or variability
○ No important uncertainty or variability</td><td>We have not sourced literature on the preferences and values of child patients and their caregivers in relation to receiving a combination of four or more behavioural interventions. However, the committee believes that since there are benefits, most children living with overweight or obesity and their caregivers would opt for this treatment.</td><td>Some children living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.</td></tr>
<tr><td colspan="3">Balance of effects
Does the balance between desirable and undesirable effects favour the intervention or the comparison?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>○ Favours the comparison
○ Probably favours the comparison
○ Does not favour either the intervention or the comparison</td><td>Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.</td><td></td></tr>
</table>

● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know		

Resources required
How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. A combination of four or more behavioural interventions are not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options (43, 44, 55). Barriers are exacerbated in rural areas, or areas of low socioeconomic status (51). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing (e.g., team uniforms). This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness
Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison	No evidence on the cost effectiveness of this intervention was identified for this population.	

o Does not favour either the intervention or the comparison o Probably favours the intervention o Favours the intervention o Varies ● No included studies		

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased ● Varies o Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Equity is affected by cost of treatments and accessibility of treatments. Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. Fees may present financial barriers for participation in extracurricular sporting activities or classes. High cost of psychological care and long wait times may make treatment prohibitive, decreasing health equity. Equity could also be addressed by raising awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration the likelihood of whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups,

		along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving a combination of four or more behavioural interventions. However, the committee believes this intervention is likely to be acceptable to the majority of children with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where intervention programmes are individually tailored and culturally and/or linguistically appropriate. Interventions should be appropriate for the developmental stage of the child. The mental health of the child should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of a combination of 4 or more behavioural interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Conditional recommendation for the intervention:
Combined multimodal (four or more) behavioural interventions may be recommended as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, et al. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: https://dx.doi.org/10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, et al. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. Journal of Clinical and Experimental Hepatology. 2022;12(3):818-29. doi: https://dx.doi.org/10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clinical Gastroenterology and Hepatology. 2019;17(8):1457-76.e7. doi: https://dx.doi.org/10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: https://doi.org/10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3

19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: https://doi.org/10.3389/fendo.2023.1069164
20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: https://doi.org/10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, et al. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: https://doi.org/10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Cohen TR, Mak IL, Loiselle S-E, Kasvis P, Hazell TJ, Vanstone CA, et al. Changes in adiposity without impacting bone health in 9- to 12-year-old children with overweight and obesity after a one-year family-centered lifestyle behavior intervention. Child Obes. 2023;19(1):46-56. doi: 10.1089/chi.2022.0008
26. Coppins DF, Margetts BM, Fa JL, Brown M, Garrett F, Huelin S. Effectiveness of a multi-disciplinary family-based programme for treating childhood obesity (The Family Project). Eur J Clin Nutr. 2011;65(8):903-9. doi: 10.1038/ejcn.2011.43
27. Kahhan N, Hossain MJ, Lang J, Harrison C, Canas J, Wysocki T, et al. Durability of changes in biomarkers of cardiometabolic disease: 1-year family-based intervention in children with obesity. Metab Syndr Relat Disord. 2021;19(5):264-71. doi: https://dx.doi.org/10.1089/met.2020.0097
28. Markert J, Herget S, Petroff D, Gausche R, Grimm A, Kiess W, et al. Telephone-based adiposity prevention for families with overweight children (T.A.F.F.-Study): one year outcome of a randomized, controlled trial. Int J Environ Res Public Health. 2014;11(10):10327-44. doi: https://dx.doi.org/10.3390/ijerph111010327
29. Stark LJ, Clifford LM, Towner EK, Filigno SS, Zion C, Bolling C, et al. A pilot randomized controlled trial of a behavioral family-based intervention with and without home visits to decrease obesity in preschoolers. J Pediatr Psychol. 2014;39(9):1001-12. doi: 10.1093/jpepsy/jsu059
30. Stark LJ, Filigno SS, Kichler JC, Bolling C, Ratcliff MB, Robson SM, et al. Maintenance following a randomized trial of a clinic and home-based behavioral intervention of obesity in preschoolers. J Pediatr. 2019;213:128-.e3. doi: https://doi.org/10.1016/j.jpeds.2019.05.004
31. Stark LJ, Spear S, Boles R, Kuhl E, Ratcliff M, Scharf C, et al. A pilot randomized controlled trial of a clinic and home-based behavioral intervention to decrease obesity in preschoolers. Obesity. 2011;19(1):134-41. doi: 10.1038/oby.2010.87
32. Taveras EM, Gortmaker SL, Hohman KH, Horan CM, Kleinman KP, Mitchell K, et al. Randomized controlled trial to improve primary care to prevent and manage childhood obesity: the High Five for Kids study. Arch Pediatr Adolesc Med. 2011;165(8):714-22. doi: 10.1001/archpediatrics.2011.44
33. Taveras EM, Marshall R, Kleinman KP, Gillman MW, Hacker K, Horan CM, et al. Comparative effectiveness of childhood obesity interventions in pediatric primary care: a cluster-randomized clinical trial. JAMA Pediatr. 2015;169(6):535-42. doi: 10.1001/jamapediatrics.2015.0182
34. Taveras EM, Marshall R, Sharifi M, Avalon E, Fiechtner L, Horan C, et al. Comparative effectiveness of clinical-community childhood obesity interventions: a randomized clinical trial. JAMA Pediatr. 2017;171(8):e171325. doi: https://dx.doi.org/10.1001/jamapediatrics.2017.1325
35. Crespo NC, Elder JP, Ayala GX, Slymen DJ, Campbell NR, Sallis JF, et al. Results of a multi-level intervention to prevent and control childhood obesity among Latino children: the Aventuras Para Ninos Study. Ann Behav Med. 2012;43(1):84-100. doi: https://dx.doi.org/10.1007/s12160-011-9332-7
36. Stettler N, Wrotniak BH, Hill DL, Kumanyika SK, Xanthopoulos MS, Nihtianova S, et al. Prevention of excess weight gain in paediatric primary care: beverages only or multiple lifestyle factors. The Smart Step Study, a cluster-randomized clinical trial. Pediatr Obes. 2015;10(4):267-74. doi: https://dx.doi.org/10.1111/ijpo.260
37. Li B, Pallan M, Liu WJ, Hemming K, Frew E, Lin R, et al. The CHIRPY DRAGON intervention in preventing obesity in Chinese primary-school--aged children: a cluster-randomised controlled trial. PLoS Med. 2019;16(11):e1002971. doi: 10.1371/journal.pmed.1002971
38. French SA, Sherwood NE, Veblen-Mortenson S, Crain AL, JaKa MM, Mitchell NR, et al. Multicomponent obesity prevention intervention in low-income preschoolers: primary and subgroup analyses of the NET-Works randomized clinical trial, 2012-2017. Am J Public Health. 2018;108(12):1695-706. doi: https://dx.doi.org/10.2105/AJPH.2018.304696

39. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: https://doi.org/10.1002/14651858.CD012691
40. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: https://doi.org/10.1111/obr.12774
41. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: https://doi.org/10.1111/obr.12866
42. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
43. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
44. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. Journal of Pediatric Nursing. 2021;57:56-72. doi: https://doi.org/10.1016/j.pedn.2020.10.025
45. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
46. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: https://doi.org/10.1111/obr.12771
47. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: https://doi.org/10.1007/s10900-020-00897-7
48. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: https://doi.org/10.3390/ijerph20010410
49. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: https://doi.org/10.1089/chi.2019.0146
50. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. Journal for Healthcare Quality. 2014;36(4):5-22. doi: https://doi.org/10.1111/jhq.12003
51. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: https://doi.org/10.1186/1479-5868-9-53
52. Strauss WJ, Nagaraja J, Landgraf AJ, Arteaga SS, Fawcett SB, Ritchie LD, et al. The longitudinal relationship between community programmes and policies to prevent childhood obesity and BMI in children: the Healthy Communities Study. Pediatr Obes. 2018;13(S1):82-92. doi: 10.1111/ijpo.12266
53. Chen P, Wang D, Shen H, Yu L, Gao Q, Mao L, et al. Physical activity and health in Chinese children and adolescents: expert consensus statement (2020). Br J Sports Med. 2020;54(22):1321-31. doi: 10.1136/bjsports-2020-102261
54. Lakka TA, Lintu N, Väistö J, Viitasalo A, Sallinen T, Haapala EA, et al. A 2 year physical activity and dietary intervention attenuates the increase in insulin resistance in a general population of children: the PANIC study. Diabetologia. 2020;63(11):2270-81. doi: 10.1007/s00125-020-05250-0
55. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782

Question: Multimodal interventions combining four or more behavioural interventions compared to treated/untreated comparators for weight maintenance/loss in children experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	multimodal interventions **combining four or more behavioural** interventions	treated/untreated **comparators**	Relative (95% CI)	**Absolute** (95% CI)		
Multimodal - four or more behavioural interventions vs untreated comparator (baseline to 12 months) – Meta analysis												
10[a]	randomised trials	serious[b]	not serious	not serious	not serious	publication bias strongly suspected[c]	1341	1047	-	Hedges' g 0.13 **lower** (0.22 lower to 0.05 lower)	⨁⨁◯◯ Low	Combining four or more interventions may result in little to no difference in adiposity.
Multimodal - four or more behavioural interventions vs untreated comparator (baseline to 12 months) – Narrative synthesis												
4[d]	randomised trials	serious[e]	serious[f]	not serious	not serious	none	4 intervention arms from 4 studies showed a positive effect of combining four or more interventions on weight maintenance/loss, 1 intervention arm from 1 study showed mixed effects				⨁⨁◯◯ Low	Combining four or more interventions may result in little to no difference in adiposity.

CI: confidence interval

Explanations

a. 10 studies, with 13 intervention arms
b. -1 using RoB-2 risk of bias rated Low (6 (18%) outcomes), Some concerns (24 (73%) outcomes), High (3 (9%) outcomes)
c. -1 Eggers test was significant =0.001
d. 4 studies, with 5 intervention arms
e. -1 using RoB-2 risk of bias rated Low (1 (14%) outcome, Some concerns (5 (83%) outcomes), High (1 (17%) outcome)
f. -1 due to unspecified heterogeneity due to differences in exposure

Adolescents (12 to <18y)

QUESTION

Should physical activity interventions vs. treated/untreated comparators be used for weight maintenance/loss in adolescents experiencing overweight or obesity?	
POPULATION:	Adolescents living with overweight or obesity
INTERVENTION:	Physical activity intervention (strengthening activities) vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u>	

Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6).

Type 2 diabetes mellitus

Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10).

Non-alcoholic fatty liver disease

Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14).

Musculoskeletal conditions

Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15).

Cancer

Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19).

Mental health

Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22).

Health-related quality of life ratings

Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23).

Reproductive health

Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated

	that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Strengthening activities intervention ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from narrative synthesis: 1 study (25) unable to be included in a meta-analysis found a favourable effect of a physical activity (strengthening activities) intervention on weight maintenance/loss. BMI increased by 0.04 kg/m^2 in the intervention arm compared to 0.59 kg/m^2 in the comparator arm. Additional desirable effects: No additional evidence from randomised controlled trials or review papers were available for desirable effects in this population for this intervention. Lived experience: No information was identified in this population specific to strength training interventions. Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, demonstrated improvements in health-related quality of life (26, 27) and reductions in mental health symptoms including depression and anxiety (28, 29). Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (30, 31). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (30, 32-34). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (30). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (30, 33, 35-37). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (30, 33, 38).	The research evidence findings are supported by evidence from multiple large community based longitudinal studies (e.g., the Cardiovascular Risks in Young Finns Study (39) and the Healthy China Action Plan (40)) that overwhelmingly support positive health outcomes of physical activity.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Strengthening activities intervention ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from meta-analyses: No evidence was identified in this population. Additional undesirable effects: No evidence was identified in this population. Lived experience:	When adolescents who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates increased physical activity, clinical judgement may be needed to balance priorities for health

	No information was identified in this population specific to strength training interventions. Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (30, 33, 36). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (30, 32, 33). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (31, 36, 41). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (33, 38). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (30, 31, 41).	care in those who are vulnerable to overexercising. A low risk of incidental musculoskeletal injury exists for adolescents with overweight or obesity during physical activity. Appropriate physical activity programs that include realistic goal setting, should be developed for young people experiencing overweight or obesity. Strategies that incorporate inclusion, engagement and awareness of weight stigma and sensitivities are needed, as this is an age when participation rates, particularly among girls, begin to decline.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Strengthening activities intervention ● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to the end of the Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from meta-analyses:</u> No evidence was identified in this population. <u>Evidence from narrative synthesis:</u> The evidence is very uncertain about the effect of this intervention on adiposity.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of adolescent patients and their caregivers in relation to receiving physical activity treatment. However, the committee believes that since there are benefits, most adolescents living with overweight or obesity and their caregivers would opt for this treatment.	Some adolescents living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Strengthening activities intervention ○ Favors the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favors the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know	Physical activity interventions are not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options, particularly for adolescent girls (30, 31, 41). These barriers were exacerbated in rural areas, or areas of low socioeconomic status (38). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing (e.g., team uniforms). Local knowledge is important for increasing accessibility to low-cost physical activity options. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate	We have not sourced literature on certainty of evidence of required resources.	

○ High ● No included studies		

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favors the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Fees for structured physical activity participation, including equipment, clothing, and classes, may be prohibitive for some people, decreasing health equity.

		Equity could be addressed by raising the awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available, low-cost physical activity programs; or when discussing the patient's care plan. Practitioners should also take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of adolescents with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where physical activity is individually tailored and appropriate. Acceptable where mental health of the adolescent is considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of physical activity interventions was not sourced. This treatment type is likely to be practicable, however, inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	**Varies**	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Physical activity interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164

20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Kennedy SG, Smith JJ, Morgan PJ, Peralta LR, Hilland TA, Eather N, et al. Implementing resistance training in secondary schools: a cluster randomized controlled trial. Med Sci Sports Exerc. 2018;50(1):62-72. doi: 10.1249/MSS.0000000000001410
26. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
27. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
28. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
29. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
30. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
31. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
32. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
33. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
34. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
35. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
36. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
37. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
38. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53
39. Telama R, Leskinen E, Yang X. Stability of habitual physical activity and sport participation: a longitudinal tracking study. Scand J Med Sci Sports. 1996;6(6):371-8. doi: 10.1111/j.1600-0838.1996.tb00109.x
40. Bao Y, Meng S, Sun Y, Jie S, Lu L. Healthy China Action plan empowers child and adolescent health and wellbeing. Lancet Public Health. 2019;4(9):e448. doi: 10.1016/S2468-2667(19)30164-1
41. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782

Question: Physical activity interventions compared to treated/untreated comparators for weight maintenance/loss in adolescents experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Physical activity* **intervention vs untreated comparator (baseline to 12 months)** – Narrative synthesis									
1[a]	randomised trials	very serious[b]	not serious	not serious	serious[c]	none	1/1 study found a favourable effect of a physical activity intervention on weight maintenance/loss BMI increased by 0.04 kg/m² in the intervention arm compared to 0.59 kg/m² in the comparator arm	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

*Strengthening activity, CI: confidence interval

Explanations

a. 1 study, with 1 intervention arm
b. -2 using RoB-2 risk of bias rated High for all outcomes
c. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should interventions combining nutrition and physical activity with or without sedentary behaviour vs. treated/untreated comparators be used for weight maintenance/loss in adolescents experiencing overweight or obesity?	
POPULATION:	Adolescents living with overweight or obesity
INTERVENTION:	Combined nutrition and physical activity interventions, with or without sedentary behaviour interventions: • Combined nutrition and physical activity interventions vs any comparator (baseline to 12 months). No sedentary behaviour interventions were identified in this population.
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9).	

Blood glucose level
Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6).

Type 2 diabetes mellitus
Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10).

Non-alcoholic fatty liver disease
Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14).

Musculoskeletal conditions
Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15).

Cancer
Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19).

Mental health
Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22).

Health-related quality of life ratings
Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23).

	<u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis</u>: From 3 studies (25-27) with 177 intervention participants and 163 comparator participants, evidence demonstrated a trivial effect size of Hedges' g 0.07 lower (0.29 lower to 0.14 higher) in the nutrition and physical activity interventions versus any comparator. <u>Additional desirable effects</u>: No additional evidence from randomised controlled trials or review papers were available for desirable effects in this population for this intervention. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (28, 29). Reductions in mental health symptoms including depression and anxiety (30, 31), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (30) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (32, 33). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (32, 34-36). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (32). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (32, 35, 37-39). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (32, 35, 40).	The benefits of weight loss or maintenance on cardiometabolic outcomes in adolescents were also considered when making judgement. The research evidence findings are supported by evidence from multiple large community based longitudinal studies (e.g., the Cardiovascular Risks in Young Finns Study (41) and the Healthy China Action Plan (42)) that overwhelmingly support positive health outcomes of improved nutrition and physical activity.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis</u>: No evidence was identified in this population. <u>Additional undesirable effects</u>: No evidence was identified in this population. <u>Lived experience</u>:	When adolescents who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates dietary change and increased physical activity, clinical judgement

	Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (32, 35, 38). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (32, 34, 35). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (33, 38, 43). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (35, 40). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (32, 33, 43).	may be needed to balance priorities for health care in those who are vulnerable to disordered eating and over-exercising. Strategies that incorporate inclusion, engagement and awareness of weight stigma and sensitivities are needed, as this is an age when participation rates, particularly among adolescent girls, are known to decline. A low risk of incidental musculoskeletal injury exists for adolescents with overweight or obesity during physical activity. Appropriate physical activity programs that include realistic goal setting, should be developed for young people experiencing overweight or obesity Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Combined nutrition and physical activity interventions may result in little to no difference in adiposity.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty	We have not sourced literature on the preferences and values of adolescent patients and their caregivers in relation to receiving combined nutrition and physical activity treatment. However, the committee believes that since there are benefits, most adolescents living with overweight or obesity and their caregivers would opt for this treatment.	Some adolescents living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

or variability ○ No important uncertainty or variability		

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition and physical activity interventions are not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options, particularly for adolescent girls (32, 33, 43). These barriers were exacerbated in rural areas, or areas of low socioeconomic status (40). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ No included studies	In a systematic review of economic evaluations of interventions targeting overweight or obesity in childhood, 14 studies of treatment-only interventions (behavioural interventions with diet and physical activity components) with adolescents were identified (44). Of these 14 interventions, study authors reported that 12 were cost effective.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living: Access to healthy food still unaffordable for disadvantaged populations. Fees for structured physical activity participation, including equipment, clothing, and classes, may be prohibitive for some people, decreasing health equity. Equity could be addressed by raising the awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available, low-cost physical activity programs; or when discussing the patient’s care plan. Practitioners should also take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when

		accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition and physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of adolescents with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where physical activity is individually tailored and appropriate. Acceptable where mental health of the adolescent is considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition and physical activity interventions was not sourced. This treatment type is likely to be practicable, however, inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation
Conditional recommendation for the intervention: Combined nutrition and physical activity interventions may be recommended as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3

19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Boyraz M, Pirgon Ö, Dündar B, Çekmez F, Hatipoğlu N. Long-term treatment with n-3 polyunsaturated fatty acids as a monotherapy in children with nonalcoholic fatty liver disease. J Clin Res Pediatr Endocrinol. 2015;7(2):121-7. doi: 10.4274/jcrpe.1749
26. Dorenbos E, Drummen M, Adam T, Rijks J, Winkens B, Martínez JA, et al. Effect of a high protein/low glycaemic index diet on insulin resistance in adolescents with overweight/obesity-a PREVIEW randomized clinical trial. Pediatr Obes. 2021;16(1):e12702. doi: 10.1111/ijpo.12702
27. Norman G, Huang J, Davila EP, Kolodziejczyk JK, Carlson J, Covin JR, et al. Outcomes of a 1-year randomized controlled trial to evaluate a behavioral 'stepped-down' weight loss intervention for adolescent patients with obesity. Pediatr Obes. 2016;11(1):18-25. doi: 10.1111/ijpo.12013
28. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
29. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
30. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
31. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
32. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
33. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
34. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
35. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
36. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
37. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
38. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
39. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
40. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53
41. Telama R, Leskinen E, Yang X. Stability of habitual physical activity and sport participation: a longitudinal tracking study. Scand J Med Sci Sports. 1996;6(6):371-8. doi: 10.1111/j.1600-0838.1996.tb00109.x

42. Bao Y, Meng S, Sun Y, Jie S, Lu L. Healthy China Action plan empowers child and adolescent health and wellbeing. Lancet Public Health. 2019;4(9):e448. doi: 10.1016/S2468-2667(19)30164-1
43. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782
44. Onyimadu O, Violato M, Astbury NM, Huls H, Heath L, Shipley A, et al. A systematic review of economic evaluations of interventions targeting childhood overweight and obesity. Obes Rev. 2023;24(9):e13597. doi: 10.1111/obr.13597

Question: Interventions combining nutrition and physical activity with or without sedentary behaviour compared to treated/untreated comparators for weight maintenance/loss in adolescents experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interventions **combining nutrition and physical activity** with or without **sedentary behaviour**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Combined nutrition and **physical activity* interventions vs any comparator (baseline to 12 months)** – Meta-**analysis**												
3[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	none	177	163	-	Hedges' g **0.07 lower** (0.29 lower to 0.14 higher)	⨁⨁◯◯ Low	Combined nutrition and physical activity interventions may result in little to no difference in adiposity.

*No sedentary behaviour interventions were identified, CI: confidence interval

Explanations

a. 3 studies, with 4 intervention arms
b. -1 using RoB-2 risk of bias rated Some concerns (8 (57%) outcomes), High (6 (43%) outcomes)
c. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)

QUESTION

Should interventions combining nutrition, physical activity and psychological vs. treated/untreated comparators be used for weight maintenance/loss in adolescents experiencing overweight or obesity?	
POPULATION:	Adolescents living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and psychological interventions vs any comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u>	

Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6).

Type 2 diabetes mellitus

Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10).

Non-alcoholic fatty liver disease

Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14).

Musculoskeletal conditions

Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15).

Cancer

Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19).

Mental health

Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22).

Health-related quality of life ratings

Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23).

Reproductive health

	Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 4 studies (25-28) with 340 intervention participants and 315 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.2 lower (95%CI 0.48 lower to 0.08 higher) in the nutrition, physical activity, and psychological intervention versus and comparator. <u>Evidence from narrative synthesis:</u> 1 additional study (29) unable to be included in the meta-analysis found a positive effect for combining nutrition, physical activity, and psychological interventions on weight maintenance/loss. The proportion of participants defined as overweight decreased by 3.65% compared to an increase of 2.17% in the comparator arm. <u>Additional desirable effects</u>: No additional evidence from randomised controlled trials or review papers were available for desirable effects in this population for this intervention. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (30, 31). Reductions in mental health symptoms including depression and anxiety (32, 33), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (32) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (34, 35). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (34, 36-38). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (34). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (34, 37, 39-41). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (34, 37, 42).	Current available data indicates a reduction in eating disorder symptoms (binge eating) with weight loss treatments. The research evidence findings are supported by evidence from multiple large community based longitudinal studies (e.g., the Cardiovascular Risks in Young Finns Study (43) and the Healthy China Action Plan (44)) that overwhelmingly support positive health outcomes of improved nutrition and physical activity.
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small	<u>Evidence from meta-analyses</u>: No evidence was identified in this population.	When adolescents who are living with overweight or

○ Moderate ○ Large ○ Varies ● Don't know	<u>Additional undesirable effects:</u> No evidence was identified in this population. <u>Lived experience</u>: Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (34, 37, 40). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (34, 36, 37). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (35, 40, 45). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (37, 42). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (34, 35, 45).	obesity are participating in a behavioural weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. A low risk of incidental musculoskeletal injury exists for adolescents with overweight or obesity during physical activity. Appropriate physical activity programs that include realistic goal setting, should be developed for young people experiencing overweight or obesity Strategies that incorporate inclusion, engagement and awareness of weight stigma and sensitivities are needed, as this is an age when participation rates, particularly among adolescent girls, are known to decline. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from meta-analysis:</u> The evidence is very uncertain about the effect of combined nutrition, physical activity, and psychological interventions on adiposity. <u>Evidence from narrative synthesis:</u> Combined nutrition, physical activity, and psychological interventions may reduce adiposity slightly.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Important uncertainty or variability o Possibly important uncertainty or variability ● Probably no important uncertainty or variability o No important uncertainty or variability	We have not sourced literature on the preferences and values of adolescent patients and their caregivers in relation to receiving combined nutrition, physical activity, and psychological treatment. However, the committee believes that since there are benefits, most adolescents living with overweight or obesity and their caregivers would opt for this treatment.	Some adolescents living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favours the intervention o Varies o Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition, physical activity and psychological interventions are not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options, particularly for adolescent girls (34, 35, 45). These barriers were exacerbated in rural areas, or areas of low socioeconomic status (42). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing (e.g., team uniforms). Long-term psychological care is often needed, and treatment is unlikely to be one-off. This treatment is likely to be cost effective but due to current resource constraints within the public health

		system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. Fees for structured physical activity participation, including equipment, clothing, and classes, may be prohibitive for some people, decreasing health equity. High cost of psychological care and long wait times may make treatment prohibitive, decreasing health equity.

		Equity could be addressed by raising the awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available, low-cost physical activity programs; or when discussing the patient's care plan. Practitioners should also take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition, physical activity, and psychological treatments. However, the committee believes this intervention is likely to be acceptable to the majority of adolescents with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where nutrition and physical activity are individually tailored and appropriate. Acceptable where mental health of the adolescent is considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition, physical activity, and psychological interventions was not sourced. This treatment type is likely to be practicable, however, inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Combined nutrition, physical activity and psychological interventions may be encouraged as part of a comprehensive approach for the management of weight related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164

20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Dâmaso AR, da Silveira Campos RM, Caranti DA, de Piano A, Fisberg M, Foschini D, et al. Aerobic plus resistance training was more effective in improving the visceral adiposity, metabolic profile and inflammatory markers than aerobic training in obese adolescents. J Sports Sci. 2014;32(15):1435-45. doi: 10.1080/02640414.2014.900692
26. Inoue DS, De Mello MT, Foschini D, Lira FS, De Piano Ganen A, Da Silveira Campos RM, et al. Linear and undulating periodized strength plus aerobic training promote similar benefits and lead to improvement of insulin resistance on obese adolescents. J Diabetes Complicat. 2015;29(2):258-64. doi: 10.1016/j.jdiacomp.2014.11.002
27. Pakpour AH, Gellert P, Dombrowski SU, Fridlund B. Motivational interviewing with parents for obesity: an RCT. Pediatrics. 2015;135(3):e644-e52. doi: 10.1542/peds.2014-1987
28. Warschburger P, Zitzmann J. Does an age-specific treatment program augment the efficacy of a cognitive-behavioral weight loss program in adolescence and young adulthood? Results from a controlled study. Nutrients. 2019;11(9):2053. doi: 10.3390/nu11092053
29. Melnyk BM, Jacobson D, Kelly SA, Belyea MJ, Shaibi GQ, Small L, et al. Twelve-month effects of the COPE Healthy Lifestyles TEEN program on overweight and depressive symptoms in high school adolescents. J Sch Health. 2015;85(12):861-70. doi: 10.1111/josh.12342
30. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
31. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
32. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
33. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
34. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
35. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
36. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
37. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
38. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
39. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
40. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
41. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
42. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53

43. Telama R, Leskinen E, Yang X. Stability of habitual physical activity and sport participation: a longitudinal tracking study. Scand J Med Sci Sports. 1996;6(6):371-8. doi: 10.1111/j.1600-0838.1996.tb00109.x
44. Bao Y, Meng S, Sun Y, Jie S, Lu L. Healthy China Action plan empowers child and adolescent health and wellbeing. Lancet Public Health. 2019;4(9):e448. doi: 10.1016/S2468-2667(19)30164-1
45. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782

Question: Interventions combining nutrition, physical activity and psychological compared to treated/untreated comparators for weight maintenance/loss in adolescents experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	interventions **combining nutrition, physical activity and psychological**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Combined nutrition, physical activity, and psychological interventions vs any comparator (baseline to 12 months) - meta-analysis												
4[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	340	315	-	Hedges' g **0.2 lower** (0.48 lower to 0.08 higher)	⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.
Combined nutrition, physical activity, and psychological interventions vs any comparator (baseline to 12 months) - narrative synthesis												
1[e]	randomised trials	very serious[f]	not serious	not serious	not serious	none	1/1 study found a positive effect for combining nutrition, physical activity, and psychological interventions on weight maintenance/ loss The proportion of participants defined as overweight decreased by 3.65% compared to an increase of 2.17% in the comparator arm				⊕⊕◯◯ Low	Combined nutrition, physical activity, and psychological interventions may reduce adiposity slightly

CI: confidence interval

Explanations

a. 4 studies, 5 intervention arms
b. -1 using RoB-2 risk of bias rated Some concerns (7 (64%) outcomes), High (4 (36%) outcomes)
c. -1 Inconsistency of I^2= 63.08%
d. -1 Imprecision due to 95% CI crosses 1
e. 1 study, with 1 intervention arm
f. -2 using RoB-2 risk of bias rated High for all outcomes

QUESTION

Should interventions combining nutrition, physical activity and family-centred vs. treated/untreated comparators be used for weight maintenance/loss in adolescents experiencing overweight or obesity?	
POPULATION:	Adolescents living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and family-centred interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u>	

Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6).

Type 2 diabetes mellitus

Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10).

Non-alcoholic fatty liver disease

Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14).

Musculoskeletal conditions

Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15).

Cancer

Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19).

Mental health

Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22).

Health-related quality of life ratings

Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23).

Reproductive health

	Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis</u>: From 1 study (25) with 180 intervention participants and 63 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.54 lower (1.18 lower to 0.11 higher) in the combined nutrition, physical activity, and family-centred interventions versus an untreated comparator. <u>Additional desirable effects</u>: No evidence was identified in this population. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (26, 27). Reductions in mental health symptoms including depression and anxiety (28, 29), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (28) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (30, 31). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (30, 32-34). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (30). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (30, 33, 35-37). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (30, 33, 38).	The research evidence findings are supported by evidence from multiple large community based longitudinal studies (e.g., the Cardiovascular Risks in Young Finns Study (39) and the Healthy China Action Plan (40)) that overwhelmingly support positive health outcomes of improved nutrition and physical activity.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> No evidence was identified in this population. <u>Additional undesirable effects:</u> No evidence was identified in this population. <u>Lived experience:</u> Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience	When adolescents who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who

	challenges in adhering to programmes due to increased stress, difficulty managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (30, 33, 36). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (30, 32, 33). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (31, 36, 41). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (33, 38). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (30, 31, 41).	are vulnerable to disordered eating and over-exercising. A low risk of incidental musculoskeletal injury exists for adolescents with overweight or obesity during physical activity. Appropriate physical activity programs that include realistic goal setting, should be developed for young people experiencing overweight or obesity. Strategies that incorporate inclusion, engagement and awareness of weight stigma and sensitivities are needed, as this is an age when participation rates, particularly among adolescent girls, are known to decline.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Combined nutrition, physical activity, and family-centred interventions may reduce adiposity.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of adolescent patients and their caregivers in relation to receiving combined nutrition, physical activity, and family-centred treatment. However, the committee believes that since there are benefits, most adolescents living with overweight or obesity and their caregivers would opt for this treatment.	Some adolescents living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition, physical activity and family-centred interventions are not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options, particularly for adolescent girls (30, 31, 41). These barriers were exacerbated in rural areas, or areas of low socioeconomic status (38). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing (e.g., team uniforms). This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living: Access to healthy food still unaffordable for disadvantaged populations. Fees for structured physical activity participation, including equipment, clothing, and classes, may be prohibitive for some people, decreasing health equity. Equity could be addressed by raising the awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available, low-cost physical activity programs; or when discussing the patient's care plan. Practitioners should also take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex,

		with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition, physical activity, and family-centred treatments. However, the committee believes this intervention is likely to be acceptable to the majority of adolescents with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where nutrition and physical activity are individually tailored and appropriate. Acceptable where mental health of the adolescent is considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition, physical activity, and family-centred interventions was not sourced. This treatment type is likely to be practicable, however, inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	**Don't know**
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

<u>Consensus statement due to limited evidence:</u>
Combined nutrition, physical activity and family-centred interventions may be recommended as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164

20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Arlinghaus KR, O'Connor DP, Johnston CA. Frequency of school-based intervention needed to improve weight outcomes of Mexican-American adolescents with overweight or obesity: a randomized controlled trial. Pediatr Obes. 2019;14(12):e12568. doi: 10.1111/ijpo.12568
26. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
27. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
28. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
29. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
30. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
31. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
32. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
33. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
34. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
35. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
36. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
37. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003
38. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53
39. Telama R, Leskinen E, Yang X. Stability of habitual physical activity and sport participation: a longitudinal tracking study. Scand J Med Sci Sports. 1996;6(6):371-8. doi: 10.1111/j.1600-0838.1996.tb00109.x
40. Bao Y, Meng S, Sun Y, Jie S, Lu L. Healthy China Action plan empowers child and adolescent health and wellbeing. Lancet Public Health. 2019;4(9):e448. doi: 10.1016/S2468-2667(19)30164-1
41. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782

Question: Interventions combining nutrition, physical activity and family-centred compared to treated/untreated comparators for weight maintenance/loss in adolescents experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	interventions **combining nutrition, physical activity and family-centred**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Combined nutrition, physical activity, and family-centred interventions vs untreated comparator (baseline to 12 months)-meta-**analysis**												
1[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	none	180	63	-	Hedges' g 0.54 **lower** (1.18 lower to 0.11 higher)	⨁⨁◯◯ Low	Combined nutrition, physical activity, and family-centred interventions may reduce adiposity.

CI: confidence interval

Explanations

a. 1 study, 3 intervention arms
b. -1 using RoB-2 risk of bias rated for all outcomes
c. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)

QUESTION

Should a combination of four or more behavioural interventions vs. treated/untreated comparators be used for weight maintenance/loss in adolescents experiencing overweight or obesity?	
POPULATION:	Adolescents living with overweight or obesity
INTERVENTION:	Combination of four or more behavioural interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with	

healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6).

Type 2 diabetes mellitus

Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10).

Non-alcoholic fatty liver disease

Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14).

Musculoskeletal conditions

Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15).

Cancer

Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19).

Mental health

Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22).

Health-related quality of life ratings

Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23).

Reproductive health

Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated

	that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from meta-analyses: From 5 studies (25-29) with 392 intervention participants and 347 comparator participants, evidence demonstrated a small effect of Hedges' g 0.42 lower (0.73 lower to 0.12 lower) in the intervention versus comparator. Additional desirable effects: No evidence was identified in this population. Lived experience: Studies of children and adolescents involved in behavioural interventions demonstrated improvements in health-related quality of life (30, 31). Reductions in mental health symptoms including depression and anxiety (32, 33), and eating disorder behaviours such as bulimia, emotional eating, and binge eating (32) were reported. Increased self-esteem and self-efficacy were identified in individuals who experienced successful behaviour changes, such as weight loss and increased fitness, which fostered increased adherence to programmes (34, 35). Supportive family dynamics and engagement of the broader family unit were shown to encourage motivation and successful behaviour change (34, 36-38). Positive relationships with healthcare providers, that were non-judgmental, supportive, and provided continuity were important (34). Tailored advice, culturally sensitive care, regular monitoring of health, and accessible programs and tools were considered enablers for adherence to behavioural interventions (34, 37, 39-41). Peer support and enjoyment of physical activities further contributed to improved mental and physical health, creating a sense of accomplishment and collaboration in achieving weight loss goals (34, 37, 42).	Less is known about the effects of multimodal approaches to weight management, due in part to study heterogeneity and low availability of evidence. However, some patients may be encouraged to take up multimodal treatments with specific tailoring to their needs. The research evidence findings are supported by evidence from multiple large community based longitudinal studies (e.g., the Cardiovascular Risks in Young Finns Study (43) and the Healthy China Action Plan (44)) that overwhelmingly support positive health outcomes of improved nutrition and physical activity. Current available data indicates a reduction in eating disorder symptoms (binge eating) with weight loss treatments.
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from meta-analyses: No evidence was identified in this population. Additional undesirable effects: No evidence was identified in this population. Lived experience: Studies of children and adolescents involved in behavioural interventions that included prescribed physical activity, reported that they experience challenges in adhering to programmes due to increased stress, difficulty	When adolescents who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who

	managing hunger, and resistance to making behavioural changes. Inaccurate beliefs and unsafe behaviours regarding weight loss, such as over-exercising were identified (34, 37, 40). Family dynamics also posed difficulties, factors such as low health literacy, cultural issues, parental separation, and negative perceptions about recommended behavioural changes caused conflict over necessary behavioural adjustments (34, 36, 37). Competing family commitments such as work, and finances of parents and caregivers impacted engagement with interventions (35, 40, 45). Negative peer perceptions about behavioural changes and bullying from peers regarding body shape and fitness levels were reported (37, 42). Insufficient facilities for engaging in exercise, lack of transportation to attend programmes and associated activities, and limited activity options also impacted participant adherence to physical activity components of interventions (34, 35, 45).	are vulnerable to disordered eating and over-exercising. A low risk of incidental musculoskeletal injury exists for adolescents with overweight or obesity during physical activity. Appropriate physical activity programs that include realistic goal setting, should be developed for young people experiencing overweight or obesity. Strategies that incorporate inclusion, engagement and awareness of weight stigma and sensitivities are needed, as this is an age when participation rates, particularly among adolescent girls, are known to decline.

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. A combination of four or more behavioural interventions may reduce adiposity slightly.	

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of adolescent patients and their caregivers in relation to receiving a combination of four or more behavioural interventions. However, the committee believes that since there are benefits, most adolescents living with overweight or obesity and their caregivers would opt for this treatment.	Some adolescents living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects
Does the balance between desirable and undesirable effects favours the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favours the intervention o Varies o Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. A combination of four or more behavioural interventions is not necessarily widely available and affordable. Structural barriers to engagement with physical activity included lack of facilities, transportation, finances, and desirable options, particularly for adolescent girls (34, 35, 45). These barriers were exacerbated in rural areas, or areas of low socioeconomic status (42). The seasonal nature of many organised sports was reported to increase sedentary behaviours during times of the year where desired activities were not offered.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Financial barriers to structured physical activity include fees for extracurricular activities or classes, equipment and clothing (e.g., team uniforms). Long-term psychological care is often needed, and treatment is unlikely to be one-off. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours the intervention o Favours the intervention o Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased ● Varies o Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity: Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. Fees for structured physical activity participation, including equipment, clothing, and classes, may be prohibitive for some people, decreasing health equity. High cost of psychological care and long wait times may make treatment prohibitive for some people, decreasing health equity. Equity could be addressed by raising the awareness of available treatments and avenues for access among patients and their caregivers. For example, highlighting locally available, low-cost physical activity programs; or

		when discussing the patient's care plan. Practitioners should also take into consideration the likelihood of extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving a combination of four or more behavioural treatments. However, the committee believes this intervention is likely to be acceptable to the majority of adolescents with overweight or obesity, their caregivers, and clinicians.	Acceptability increases where nutrition and physical activity are individually tailored and appropriate. Acceptable where mental health of the adolescent is considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of a combination of four or more behavioural interventions was not sourced. This treatment type is likely to be practicable, however, inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
	○	○	●	○

CONCLUSIONS

Recommendation

Conditional recommendation for the intervention:

Combined multimodal (four or more) behavioural interventions may be recommended as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3

19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Alustiza E, Perales A, Mateo-Abad M, Ozcoidi I, Aizpuru G, Albaina O, et al. Tackling risk factors for type 2 diabetes in adolescents: PRE-STARt study in Euskadi. An Pediatr (Barc). 2021;95(3):186-96. doi: 10.1016/j.anpede.2020.11.005
26. DeBar LL, Stevens VJ, Perrin N, Wu P, Pearson J, Yarborough BJ, et al. A primary care-based, multicomponent lifestyle intervention for overweight adolescent females. Pediatrics. 2012;129(3):e611-e20. doi: 10.1542/peds.2011-0863
27. Pakpour AH, Gellert P, Dombrowski SU, Fridlund B. Motivational interviewing with parents for obesity: an RCT. Pediatrics. 2015;135(3):e644-e52. doi: 10.1542/peds.2014-1987
28. Savoye M, Nowicka P, Shaw M, Yu S, Dziura J, Chavent G, et al. Long-term results of an obesity program in an ethnically diverse pediatric population. Pediatrics. 2011;127(3):402-10. doi: 10.1542/peds.2010-0697
29. Vos RC, Huisman SD, Houdijk ECAM, Pijl H, Wit JM. The effect of family-based multidisciplinary cognitive behavioral treatment on health-related quality of life in childhood obesity. Qual Life Res. 2012;21(9):1587-94. doi: 10.1007/s11136-011-0079-1
30. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6:CD012691. doi: 10.1002/14651858.CD012691
31. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89. doi: 10.1111/obr.12774
32. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
33. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Association of pediatric obesity treatment, including a dietary component, with change in depression and anxiety: a systematic review and meta-analysis. JAMA Pediatr. 2019;173(11):e192841-e. doi: 10.1001/jamapediatrics.2019.2841
34. Lang S, Gibson S, Ng KW, Truby H. Understanding children and young people's experiences pursuing weight loss maintenance using the Socio-ecological Model: a qualitative systematic literature review. Obes Rev. 2021;22(5):e13172. doi: 10.1111/obr.13172
35. Roberts KJ, Binns HJ, Vincent C, Koenig MD. A scoping review: family and child perspectives of clinic-based obesity treatment. J Pediatr Nurs. 2021;57:56-72. doi: 10.1016/j.pedn.2020.10.025
36. de Jong M, Jansen N, van Middelkoop M. A systematic review of patient barriers and facilitators for implementing lifestyle interventions targeting weight loss in primary care. Obes Rev. 2023;24(8):e13571. doi: 10.1111/obr.13571
37. Jones HM, Al-Khudairy L, Melendez-Torres GJ, Oyebode O. Viewpoints of adolescents with overweight and obesity attending lifestyle obesity treatment interventions: a qualitative systematic review. Obes Rev. 2019;20(1):156-69. doi: 10.1111/obr.12771
38. Tamayo MC, Dobbs PD, Pincu Y. Family-centered interventions for treatment and prevention of childhood obesity in hispanic families: a systematic review. J Community Health. 2021;46(3):635-43. doi: 10.1007/s10900-020-00897-7
39. Fidjeland TG, Øen KG. Parents' experiences using digital health technologies in paediatric overweight and obesity support: an integrative review. Int J Environ Res Public Health. 2022;20(1). doi: 10.3390/ijerph20010410
40. McMaster CM, Gow ML, Neal R, Alexander S, Baur LA, Cohen J. Acceptability of hospital-based pediatric weight management services among patients and families: a narrative synthesis. Child Obes. 2020;16(2):129-40. doi: 10.1089/chi.2019.0146
41. Skelton JA, Irby MB, Geiger AM. A systematic review of satisfaction and pediatric obesity treatment: new avenues for addressing attrition. J Healthc Qual. 2014;36(4):5-22. doi: 10.1111/jhq.12003

42. Stankov I, Olds T, Cargo M. Overweight and obese adolescents: what turns them off physical activity? Int J Behav Nutr Phys Act. 2012;9:53. doi: 10.1186/1479-5868-9-53
43. Telama R, Leskinen E, Yang X. Stability of habitual physical activity and sport participation: a longitudinal tracking study. Scand J Med Sci Sports. 1996;6(6):371-8. doi: 10.1111/j.1600-0838.1996.tb00109.x
44. Bao Y, Meng S, Sun Y, Jie S, Lu L. Healthy China Action plan empowers child and adolescent health and wellbeing. Lancet Public Health. 2019;4(9):e448. doi: 10.1016/S2468-2667(19)30164-1
45. Arai L, Panca M, Morris S, Curtis-Tyler K, Lucas PJ, Roberts HM. Time, monetary and other costs of participation in family-based child weight management interventions: qualitative and systematic review evidence. PLoS ONE. 2015;10(4):e0123782. doi: 10.1371/journal.pone.0123782

Question: Multimodal interventions combining four or more behavioural interventions compared to treated/untreated comparators for weight maintenance/loss in adolescents experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	multimodal interventions combining four or more behavioural interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Multimodal - four or more behavioural interventions vs untreated comparator (baseline to 12 months) – Meta analysis												
5[a]	randomised trials	serious[b]	serious[c]	not serious	not serious	none	392	347	-	Hedges' g 0.42 **lower** (0.73 lower to 0.12 lower)	⨁⨁◯◯ Low	A combination of four or more interventions may reduce adiposity slightly

CI: confidence interval

Explanations

a. 5 studies, with 5 intervention arms
b. -1 using RoB-2 risk of bias rated Low (6 (43%) outcomes), Some concerns (8 (57%) outcomes)
c. -1 Inconsistency of I2=77.92%

QUESTION

Should pharmacological interventions vs. treated/untreated comparators be used for weight maintenance/loss in adolescents experiencing overweight or obesity?	
POPULATION:	Adolescents living with overweight or obesity
INTERVENTION:	Pharmacological interventions: **Pharmacological interventions for the treatment of overweight or obesity** • Anorectic and Anticonvulsant drug class interventions vs any comparator (baseline to end-point) • Phentermine, 7.5mg plus Topiramate, 46.0mg per day intervention vs any comparator (baseline to final end-point) • Phentermine, 15.0mg plus Topiramate, 92.0mg per day intervention vs any comparator (baseline to final end-point) • Glucagon-like peptide-1 receptor agonists drug class interventions vs any comparator (baseline to final end-point) • Liraglutide, 3.0mg per day (subcutaneous) intervention vs any comparator (baseline to final end-point) • Semaglutide, 2.4mg per week (subcutaneous) intervention vs any comparator (baseline to final end-point)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Guideline Development Committee members with potential Conflicts of Interest as detailed in 'Management of competing interests' section of the Guideline document participated in discussions but were not part of final recommendation development.

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or	

obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7).

Cardiovascular disease

Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9).

Blood glucose level

Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6).

Type 2 diabetes mellitus

Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10).

Non-alcoholic fatty liver disease

Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14).

Musculoskeletal conditions

Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15).

Cancer

Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19).

Mental health

Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21).

	Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Drugs approved for weight management: ○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	**Pharmacological interventions approved for the treatment of overweight or obesity (by drug class and drug type, where applicable):** **<u>Anorectic and anticonvulsant drug class</u>** <u>Evidence from meta-analysis</u>: From 1 study (25) with 167 intervention participants and 56 comparator participants, evidence demonstrated a large effect size of Hedges' g 1.17 lower (95% CI 1.48 lower to 0.86 lower) in anorectic and anticonvulsant drug class interventions versus any comparator. <u>Evidence from narrative synthesis:</u> Additional evidence from 1 study (25) that was unable to be included in a meta-analysis found a positive effect of phentermine, 7.5mg plus topiramate, 46.0mg per day on weight maintenance/loss. BMI decreased by 2.53kg/m^2 in the intervention arm versus an increase of 1.20kg/m^2 in the comparator/placebo arm. <u>Evidence from narrative synthesis:</u> Additional evidence from 1 study (25) that was unable to be included in a meta-analysis found a positive effect of phentermine, 15.0mg plus topiramate, 92.0mg per day on weight maintenance/loss. BMI decreased by 4.15kg/m^2 in the intervention arm compared to an increase of 1.20kg/m^2 in the comparator/placebo arm. **<u>Glucagon-like peptide-1 receptor agonists drug class</u>** <u>Evidence from narrative synthesis</u>: 2 additional studies (25, 26) unable to be included in the meta-analysis found a positive effect of glucagon-like peptide-1 receptor agonists drug class on weight maintenance/loss. 1 additional study (27) unable to be included in the meta-analysis found a positive effect of liraglutide, 3.0mg per day (subcutaneous)	Clinicians should be aware that each drug class has a different profile of additional benefits which may be relevant when prescribing. Weight loss is typically lower in people living with Type 2 diabetes mellitus compared to those without diabetes mellitus, however health benefits are still experienced. Some drugs used for treatment of Type 2 diabetes mellitus (e.g. semaglutide, liraglutide) are prescribed in lower dosages than for the treatment of obesity, however patients may have weight loss benefits at these dosages. NOTE: Studies of other pharmacological interventions commonly used by clinicians for weight management/loss exist, however these studies did not qualify for inclusion in this review.

	interventions on weight maintenance/loss. BMI-SDS decreased by 0.23 in the intervention arm versus no change, 0.00, in the comparator/placebo arm. 1 additional study (26) unable to be included in the meta-analysis found a positive effect of semaglutide, 2.4mg per week (subcutaneous) on weight maintenance/loss. BMI decreased by 16.1% in the intervention arm versus an increase of 0.1% in the comparator/placebo arm. <u>Additional desirable effects</u>: No evidence was identified in this population. <u>Lived experience:</u> No evidence was identified in this population.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Pharmacological interventions approved for weight management: ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis:</u> No evidence was identified in this population. <u>Additional undesirable effects</u>: No evidence was identified in this population. <u>Lived experience:</u> No evidence was identified in this population.	Clinicians should be aware each drug class has a different profile of adverse effects, which may be relevant when prescribing. Pharmacological intervention-related adverse effects are common, most are mild and often transient. Many adverse effects can be minimised or mitigated by starting at a low dose followed by a gradual increase. Regular review of medication and long-term follow-up are necessary. Awareness of possible drug-drug interactions is necessary. These differ by drug class. There is very limited long-term data from pharmacotherapy studies. Need for regular revision of evidence. In addition to intentional adiposity loss, some children living with overweight or obesity may experience a slowing down of bone accretion.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

Pharmacological interventions approved for weight management: ○ Very low ○ Low ● Moderate ● High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. **<u>Evidence from meta-analysis of pharmacological interventions approved for the treatment of overweight or obesity:</u>** **Anorectic and anticonvulsant drug class interventions result in a large reduction in adiposity.** Phentermine, 7.5mg plus topiramate, 46.0mg per day results in a reduction in adiposity. Phentermine, 15.0mg plus topiramate, 92.0mg per day results in a reduction in adiposity. **<u>Evidence from narrative synthesis of pharmacological interventions approved for the treatment of overweight or obesity:</u>** The following interventions likely reduce adiposity: • Glucagon-like peptide-1 receptor agonists drug class • Liraglutide, 3.0mg per day (subcutaneous) • Semaglutide, 2.4mg per week (subcutaneous)	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of adolescent patients and their caregivers in relation to receiving pharmacological intervention. However, the committee believes that since there are benefits, most adolescents living with overweight or obesity and their caregivers would opt for this treatment, where clinically appropriate.	A lack of availability for people who meet treatment guidelines has highlighted the widespread demand/unmet need for pharmacological interventions. Some adolescents living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Pharmacological interventions approved for weight management: ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention.	

○ Varies ○ Don't know		

Resources required
How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resource requirements for pharmacological interventions for overweight or obesity.	Currently there is no subsidisation of pharmacological interventions by the PBS, and the entire treatment cost is covered by patients. This treatment is likely to be cost effective but due to current resource constraints within the public health system, treatment access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness
Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ● Varies ○ No included studies	Cost effectiveness data is presented by study rather than by medication because studies differ in what inputs they used (e.g., medication effectiveness data, estimates of associations between BMI and quality of life) and their time horizons. Note that quality adjusted life years (QALYs) are calculated using estimates of the change in QALYs per BMI unit lost (i.e., this figure is constant throughout calculations in a given study) and change in BMI with various pharmaceutical interventions. Therefore, QALYs are a proxy for the effectiveness of pharmaceutical interventions. In a cost-effectiveness analysis from a US perspective (28), the QALYs gained over a 5-year time horizon were 3.18 years for semaglutide, 3.10 years for liraglutide, 3.12 years for mid-dose phentermine plus topiramate (7.5/46mg daily), and 3.13 years for top-dose phentermine plus topiramate (15/92mg daily). The change in QALYs with behavioural counselling was 3.07 years.	

	In a cost-effectiveness analysis from a US perspective (29), the QALYs gained over a 10-year time horizon were 7.85 years for semaglutide (2.4mg weekly, subcutaneous), 7.78 years for liraglutide (3.0mg daily, subcutaneous), 7.77 years for phentermine plus topiramate extended-release (15mg/92mg daily), and 7.75 years for orlistat (120mg 3 times daily). The change in QALYs with no treatment was 7.69 years.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention. Widely available and accessible pharmacological interventions increase health equity.	Current drug costs and reimbursement structures of medications are a barrier to equity. When discussing the patient's care plan, practitioners should take into consideration the likelihood of out-of-pocket expenses (i.e. gap payments) when accessing the prescribed treatment, etc. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Large barriers to accessibility of pharmacological interventions exist for many people. Self-funded treatment decreases equity.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes	We have not sourced literature on the acceptability of receiving pharmacological interventions. However, the committee believes this intervention is likely to be acceptable to the majority of adolescents with overweight or obesity, their caregivers, and clinicians, where clinically appropriate.	Stigma may reduce acceptability of this treatment to patients and clinicians.

○ Varies ○ Don't know		Some patients, caregivers or clinicians may not deem pharmacological interventions for weight management in adolescents to be acceptable. Acceptability increases where interventions (including adjunct interventions) are individually tailored and culturally appropriate. For example: accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of pharmacological interventions was not sourced. This treatment type is likely to be practicable, however, inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Medication shortages and supply issues may decrease feasibility of pharmacological interventions. Current pharmacological intervention costs and reimbursement structures of medications are a barrier to feasibility. Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	**High**			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or** variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	**Varies**	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

CONCLUSIONS

Recommendation
Strong recommendation for the intervention: Pharmacological interventions, **approved** by the TGA for weight management, should be considered, where clinically appropriate, as part of a comprehensive treatment program to improve weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164

20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Kelly AS, Bensignor MO, Hsia DS, Shoemaker AH, Shih W, Peterson C, et al. Phentermine/topiramate for the treatment of adolescent obesity. NEJM Evidence. 2022;1(6). doi: 10.1056/EVIDoa2200014
26. Weghuber D, Barrett T, Barrientos-Perez M, Gies I, Hesse D, Jeppesen OK, et al. Once-Weekly Semaglutide in Adolescents with Obesity. N Engl J Med. 2022;387(24):2245-57.
27. Kelly AS, Auerbach P, Barrientos-Perez M, Gies I, Hale PM, Marcus C, et al. A randomized, controlled trial of liraglutide for adolescents with obesity. N Engl J Med. 2020;382(22):2117-28. doi: 10.1056/NEJMoa1916038
28. Lim F, Bellows BK, Tan SX, Aziz Z, Woo Baidal JA, Kelly AS, Hur C. Cost-Effectiveness of Pharmacotherapy for the Treatment of Obesity in Adolescents. JAMA Netw Open. 2023;6(8):e2329178. doi: 10.1001/jamanetworkopen.2023.29178
29. Mital S, Nguyen HV. Cost-Effectiveness of Antiobesity Drugs for Adolescents With Severe Obesity. JAMA Netw Open. 2023;6(10):e2336400. doi: 10.1001/jamanetworkopen.2023.36400

Question: Pharmacological interventions compared to treated/untreated comparators for weight maintenance/loss in adolescents experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pharmacological interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Anorectic and Anticonvulsant drug class interventions vs any comparator (baseline to end-point) - meta-analysis												
1[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	very strong association	167	56	-	Hedges' g 1.17 **lower** (1.48 lower to 0.86 lower)	⊕⊕⊕⊕ High	Anorectic and Anticonvulsant drug class interventions result in a large reduction in adiposity.
Phentermine, 7.5mg plus Topiramate, 46.0mg per day intervention vs any comparator (baseline to final end-point) - narrative synthesis												
1[d]	randomised trials	serious[b]	not serious	not serious	serious[c]	very strong association	1/1 study found a positive effect of phentermine, 7.5mg plus topiramate, 46.0mg per day on weight maintenance/loss. BMI decreased by 2.53kg/m[2] in the intervention arm versus an increase of 1.20kg/m[2] in the comparator/placebo arm.				⊕⊕⊕⊕ High	Phentermine, 7.5mg plus Topiramate, 46.0mg per day results in a reduction in adiposity
Phentermine, 15.0mg plus Topiramate, 92.0mg per day intervention vs any comparator (baseline to final end-point) - narrative synthesis												
1[d]	randomised trials	serious[b]	not serious	not serious	serious[c]	very strong association	1/1 study found a positive effect of phentermine, 15.0mg plus topiramate, 92.0mg per day on weight maintenance/loss. BMI decreased by 4.15kg/m[2] in the intervention arm compared to an increase of 1.20kg/m[2] in the comparator/placebo arm.				⊕⊕⊕⊕ High	Phentermine, 15.0mg plus Topiramate, 92.0mg per day results in a reduction in adiposity
Glucagon-like peptide-1 receptor agonists drug class interventions vs any comparator (baseline to final end-point) - narrative synthesis												
2[e]	randomised trials	not serious	serious[f]	not serious	not serious	none	2/2 studies found a positive effect of glucagon-like peptide-1 receptor agonists drug class on weight maintenance/loss				⊕⊕⊕◯ Moderate	Glucagon-like peptide-1 receptor agonists drug class interventions likely reduce adiposity.
Liraglutide, 3.0mg per day (sc) intervention vs any comparator (baseline to final end-point) - narrative synthesis												
1[d]	randomised trials	not serious	not serious	not serious	serious[c]	none	1/1 study found a positive effect of liraglutide, 3.0mg per day (subcutaneous) interventions on weight maintenance/loss BMI-SDS decreased by 0.23 in the intervention arm versus no change, 0.00, in the comparator/placebo arm.				⊕⊕⊕◯ Moderate	Liraglutide, 3.0mg per day (subcutaneous) likely reduces adiposity
Semaglutide, 2.4mg per week (subcutaneous) intervention vs any comparator (baseline to final end-point) - narrative synthesis												
1[d]	randomised trials	not serious	not serious	not serious	serious[c]	none	1/1 study found a positive effect of semaglutide, 2.4mg per week (subcutaneous) on weight maintenance/loss. BMI decreased by 16.1% in the intervention arm versus an increase of 0.1% in the comparator/placebo arm.				⊕⊕⊕◯ Moderate	Semaglutide, 2.4mg per week (subcutaneous) likely reduces adiposity.

CI: confidence interval

Explanations

a. 1 study, with 2 intervention arms
b. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
c. -1 Imprecision due to small sample size (Total n<400)
d. 1 study, with 1 intervention arm
e. 2 studies, with 2 intervention arms
f. -1 for unspecified heterogeneity due to differences in exposure
g. -2 using RoB-2 risk of bias rated High for all outcomes
h. -2 Imprecision due to very small size (Total n<50)

QUESTION

Should surgical interventions vs. treated/untreated comparators be used for weight maintenance/loss in adolescents experiencing overweight or obesity?	
POPULATION:	Adolescents living with overweight or obesity
INTERVENTION:	Surgical interventions: • **Bariatric surgery intervention vs medical treatment (baseline to final end-point)** • Laparoscopic adjustable gastric banding (LAGB) vs medical treatment (baseline to final end-point) • Laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic vertical sleeve gastrectomy vs medical treatment (baseline to final end-point)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Guideline Development Committee members with potential Conflicts of Interest as detailed in 'Management of competing interests' section of the Guideline document participated in discussions but were not part of final recommendation development.

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in children and adolescents. <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also	

	had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic	

	ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Bariatric surgery versus medical treatment: ○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	**Bariatric surgery versus medical treatment:** <u>Evidence from meta-analysis:</u> From 2 studies (25, 26) with 49 intervention participants and 48 comparator participants, evidence demonstrated a large effect size of Hedges' g 2.27 lower (2.79 lower to 1.76 lower) in bariatric surgery interventions versus medical treatment. <u>Evidence from narrative synthesis:</u> 1 additional study (26) unable to be included in the meta-analysis found a positive effect of laparoscopic adjustable gastric banding (LAGB) on weight loss/maintenance. BMI decreased in the intervention arm by 12.7 kg/m^2 compared to a decrease of 1.3 kg/m^2 in the comparator arm. 1 additional study (25) unable to be included in the meta-analysis found a positive effect of Laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic vertical sleeve gastrectomy on weight loss/maintenance. BMI decreased by 12.7 kg/m^2 in the intervention arm compared to 1.1 kg/m^2 in the comparator arm. <u>Additional desirable effects:</u> Favourable outcomes for adolescents who underwent bariatric surgery included increased remission of metabolic syndrome and improved physical function (a HRQoL component) (27). <u>Lived experience</u>: Health-related quality of life increases (28-32) and reduction in depressive symptoms (28, 30, 33, 34) following bariatric surgery interventions were identified.	The Teen-LABS study of 242 adolescents who received bariatric surgery showed, by 3 years, that remission of Type 2 diabetes mellitus occurred in 95% of those with the condition at baseline, remission of prediabetes in 76%, remission of elevated blood pressure in 74% and remission of dyslipidaemia in 66% (35). There were also improvements in health-related quality of life. The Teen-LABS study reported improvements from baseline in health-related quality of life at 3 years post-surgery.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Bariatric surgery versus medical treatment: ○ Trivial ● Small ○ Moderate ○ Large	<u>Evidence from meta-analyses:</u> No evidence was identified in this population. <u>Additional undesirable effects</u>: No evidence was identified in this population. <u>Additional undesirable effects:</u>	In addition to intentional adiposity loss, some adolescents living with overweight or obesity may experience a slowing down of bone accretion.

○ Varies ○ Don't know	Adolescents who underwent bariatric surgery experienced surgery-related adverse events (six proximal gastric enlargements and two needlestick injuries to tubing among 25 adolescents) (27). <u>Lived experience:</u> No evidence on the lived experience perspectives for bariatric surgery was identified for this population	The Teen-LABS study reported that 1.9% (i.e. 3 of 161 participants) of adolescents had died within 5 years of having gastric bypass surgery (35). Two of these deaths were consistent with overdose. Long term increased risk of vitamin and mineral deficiencies, and osteoporosis following surgery.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Bariatric surgery versus medical treatment: ○ Very low ○ Low ○ Moderate ● High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Bariatric surgery results in a large reduction in adiposity. Laparoscopic adjustable gastric banding results in a large reduction in adiposity. Laparoscopic Roux-en-Y gastric bypass results in a large reduction in adiposity.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of adolescents living with obesity in relation to receiving bariatric surgery. However, the committee believes that since there are benefits, most adolescents living with moderate to severe obesity and their caregivers would opt for this treatment, where clinically appropriate.	The lived experience perspective supports this judgement. Some adolescents living with overweight or obesity and their caregivers (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

Bariatric surgery versus medical treatment: o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours the intervention ● Favours the intervention o Varies o Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies o Don't know	We have not sourced literature on the resource requirements for bariatric surgery.	Surgical treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Resources required will depend on setting, the intervention to be provided, and who provides it. The committee's view is there are large upfront costs, however there are large savings. Bariatric surgery procedures are mostly carried out in the private health sector in Australia.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ No included studies	Bariatric surgery incurs substantial initial costs. Cost effectiveness analyses have consistently modelled bariatric surgery as a cost-effective treatment for obesity management in adults when compared to usual care/non-surgical treatments, however, data on bariatric surgery for adolescents are extremely limited making it difficult to draw conclusions on cost-effectiveness in this population. Three available cost-effectiveness studies found bariatric surgery could be a cost-effective treatment for adolescents with severe obesity if assessed over longer time periods (>3-5 years). One cost-effectiveness analysis of a US study found an incremental cost-effectiveness ratio of USD$154,684 per quality-adjusted life-year (QALY) when assessed over 3 years, USD$114,078 per QALY over 4 years, and USD$91,032 per QALY over 5 years (36). Thus, bariatric surgery is cost-effective at 5 years using a willingness-to-pay threshold of USD$100,000 per QALY. One cost-effectiveness analysis from the UK compared sleeve gastrectomy with no surgery (37). The incremental cost/QALY was GBP£,1978 (95% CI GBP£1,954-2,002) for males and GBP£1,941 (95% CI GBP£1,915-1969) for females. Bariatric surgery in adolescents with severe obesity was found to be cost-effective. One cost-effectiveness analysis from the US found bariatric surgery was not cost-effective in the first three years using a threshold of a USD$100,000/QALY (38). Surgery became cost-effective after that (USD$80,065/QALY in year four and USD$36,570/QALY in year seven).	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Current treatment costs and reimbursement structures for surgical treatment are a barrier to equity. When discussing the patient's care plan, practitioners should take into consideration Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these

		populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving bariatric surgery among adolescents. However, the committee believes this intervention is likely to be acceptable to the majority of adolescents with moderate to severe obesity, their caregivers, and clinicians, where it is clinically appropriate.	Some patients, caregivers or clinicians may not deem surgical interventions for weight management in adolescents to be acceptable. Mental health of the participant should be considered and monitored.

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of bariatric surgery interventions was not sourced. This treatment type is likely to be practicable, however, inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Bariatric surgery is not widely available to adolescents in Australia. Lack of availability to adolescents in the public health sector in most states limits feasibility. Resourcing will be dependent on setting, intervention, location and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	**High**			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	**Large costs**	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

CONCLUSIONS

Recommendation

Strong recommendation for the intervention:

For adolescents with severe obesity, healthcare professionals should consider bariatric surgery interventions as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3

19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Järvholm K, Janson A, Peltonen M, Neovius M, Gronowitz E, Engström M, et al. Metabolic and bariatric surgery versus intensive non-surgical treatment for adolescents with severe obesity (AMOS2): a multicentre, randomised, controlled trial in Sweden. Lancet Child Adolesc Health. 2023;7(4):249-60. doi: 10.1016/S2352-4642(22)00373-X
26. O'Brien PE, Sawyer SM, Laurie C, Brown WA, Skinner S, Veit F, et al. Laparoscopic adjustable gastric banding in severely obese adolescents: a randomized trial. JAMA. 2010;303(6):519-26. doi: 10.1001/jama.2010.81
27. Ells LJ, Mead E, Atkinson G, Corpeleijn E, Roberts K, Viner R, et al. Surgery for the treatment of obesity in children and adolescents. Cochrane Database Syst Rev. 2015(6):CD011740. doi: 10.1002/14651858.CD011740
28. Trooboff SW, Stucke RS, Riblet NB, Kulkarni AS, Anand R, Casey A, Hofley MA. Psychosocial outcomes following adolescent metabolic and bariatric surgery: a systematic review and meta-analysis. Obes Surg. 2019;29(11):3653-64. doi: 10.1007/s11695-019-04048-3
29. Steele RG, Gayes LA, Dalton WTI, Smith C, Maphis L, Conway-Williams E. Change in health-related quality of life in the context of pediatric obesity interventions: a meta-analytic review. Health Psychol. 2016;35(10):1097-109. doi: 10.1037/hea0000362
30. White B, Doyle J, Colville S, Nicholls D, Viner RM, Christie D. Systematic review of psychological and social outcomes of adolescents undergoing bariatric surgery, and predictors of success. Clin Obes. 2015;5(6):312-24. doi: 10.1111/cob.12119
31. Black JA, White B, Viner RM, Simmons RK. Bariatric surgery for obese children and adolescents: a systematic review and meta-analysis. Obes Rev. 2013;14(8):634-44. doi: 10.1111/obr.12037
32. Willcox K, Brennan L. Biopsychosocial outcomes of laparoscopic adjustable gastric banding in adolescents: a systematic review of the literature. Obes Surg. 2014;24(9):1510-9. doi: 10.1007/s11695-014-1273-3
33. Hillstrom KA, Graves JK. A review of depression and quality of life outcomes in adolescents post bariatric surgery. J Child Adolesc Psychiatr Nurs. 2015;28(1):50-9. doi: 10.1111/jcap.12104
34. Herget S, Rudolph A, Hilbert A, Blüher S. Psychosocial status and mental health in adolescents before and after bariatric surgery: a systematic literature review. Obes Facts. 2014;7(4):233-45. doi: 10.1159/000365793
35. Inge TH, Courcoulas AP, Jenkins TM, Michalsky MP, Helmrath MA, Brandt ML, et al. Weight Loss and Health Status 3 Years after Bariatric Surgery in Adolescents. N Engl J Med. 2016;374(2):113-23. doi: 10.1056/NEJMoa1506699
36. Bairdain S, Samnaliev M. Cost-effectiveness of Adolescent Bariatric Surgery. Cureus. 2015;7(2):e248. doi: 10.7759/cureus.248
37. Panca M, Viner RM, White B, Pandya T, Melo H, Adamo M, et al. Cost-effectiveness of bariatric surgery in adolescents with severe obesity in the UK. Clin Obes. 2018;8(2):105-13. doi: 10.1111/cob.12232
38. Klebanoff MJ, Chhatwal J, Nudel JD, Corey KE, Kaplan LM, Hur C. Cost-effectiveness of Bariatric Surgery in Adolescents With Obesity. JAMA Surg. 2017;152(2):136-41. doi: 10.1001/jamasurg.2016.3640

Question: Surgical interventions compared to treated/untreated comparators for weight maintenance/loss in adolescents experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**surgical** interventions	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Bariatric surgery intervention vs best medical treatment (baseline to final end-point) - Meta-**analysis**												
2[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	very strong association	49	48	-	Hedges' g 2.27 lower (2.79 lower to 1.76 lower)	⊕⊕⊕⊕ High	Bariatric surgery results in a large reduction in adiposity
Laparoscopic adjustable gastric banding (LAGB) vs best medical treatment (baseline to final end-point) - Narrative synthesis												
1[d]	randomised trials	serious[e]	not serious	not serious	serious[c]	very strong association	1/1 studies found a positive effect of Laparoscopic adjustable gastric banding (LAGB) on weight loss/maintenance. BMI decreased in the intervention arm by 12.7kg/m^2 compared to a decrease of 1.3kg/m^2 in the comparator arm.				⊕⊕⊕⊕ High	Laparoscopic adjustable gastric banding (LAGB) results in a large reduction in adiposity
Laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic vertical sleeve gastrectomy vs best medical treatment (baseline to final end-point) - Narrative synthesis												
1[d]	randomised trials	not serious	not serious	not serious	very serious[f]	very strong association	1/1 study found a positive effect of Laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic vertical sleeve gastrectomy on weight loss/maintenance BMI decreased by 12.7kg/m^2 in the intervention arm compared to 1.1kg/m^2 in the comparator arm.				⊕⊕⊕⊕ High	Laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic vertical sleeve gastrectomy results in a large reduction in adiposity

CI: confidence interval

Explanations

a. 2 studies, with 2 intervention arms
b. -1 using RoB-2 risk of bias rated Low (3 (30%) outcomes), Some concerns (7 (70%) outcomes)
c. -1 Imprecision due to small sample size (Total n<400)
d. 1 study, with 1 intervention arm
e. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
f. -2 Imprecision due to very small size (Total n<50)

Young and middle-aged adults (18 to <65y)

QUESTION

Should nutrition interventions vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Nutrition interventions: • Nutrition intervention vs untreated comparator (baseline to 12 months) • Dietary approaches with no specific daily energy intake goal vs untreated comparator (baseline to 12 months) • Nutrition interventions with a daily energy intake goal vs untreated comparator (baseline to 12 months) • Nutrition interventions with a daily energy intake goal followed by dietary approaches with no specific daily energy intake goal vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25).	

	<u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41). Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45). <u>Non-alcoholic fatty liver disease</u> Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51). Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52). <u>Musculoskeletal conditions</u> Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56). <u>Cancer</u> When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)). Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132).	

	Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Nutrition intervention overall ○ Trivial ○ Small	<u>Evidence from meta-analyses:</u> From 15 studies (177-191) with 1362 intervention participants and 1106 comparator participants, evidence demonstrated a moderate effect size	In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e.

● Moderate ○ Large ○ Varies ○ Don't know **Dietary approaches with no specific daily energy intake goal** ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know **Nutrition interventions with a daily energy intake goal** ○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know **Nutrition interventions with a daily energy intake goal followed by dietary approaches with no specific daily energy intake goal** ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Hedges' g 0.47 lower (95%CI 0.76 lower to 0.18 lower) in the intervention versus untreated comparator in nutrition interventions. Evidence from meta-analyses: From 8 studies (182, 184-187, 189, 190, 192) with 695 intervention participants and 643 comparator participants, evidence demonstrated a trivial effect size Hedges' g 0.16 lower (95%CI 0.3 lower to 0.03 lower) in the intervention versus untreated comparator in dietary approaches with no specific daily energy intake goal. Evidence from narrative synthesis: 1 additional study (193) found dietary approaches with no specific daily energy intake goal may reduce adiposity slightly. Evidence from meta-analyses: From 4 studies (180, 181, 183, 188) with 476 intervention participants and 268 comparator participants, evidence demonstrated a large effect size Hedges' g 0.87 lower (95%CI 1.72 lower to 0.03 lower) in the intervention versus untreated comparator in nutrition interventions with a daily energy intake goal. Evidence from meta-analyses: From 3 studies (177-179) with 191 intervention participants and 195 comparator participants, evidence demonstrated a moderate effect size Hedges' g 0.77 lower (95%CI 1.84 lower to 0.31 higher) in the intervention versus untreated comparator in nutrition interventions with a daily energy intake goal followed by dietary approaches with no specific daily energy intake goals. Additional desirable effects: Additional favourable outcomes of nutrition interventions in young and middle-aged adults were improved type 2 diabetes risk (with energy restriction interventions and ad libitum dietary interventions) (42), fasting plasma glucose (very low energy diet [VLED] versus low energy diet [LED]) (194), fasting insulin (with low GI diets) (195), HDL-C (with commercial weight loss programmes (196) and low GI diets (195)), and triglycerides (with commercial weight loss programmes (196)). For men undertaking nutrition interventions, there were additional beneficial outcomes including increased HDL-C and reduced triglycerides (197). Lived experience: Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical	fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (223).

	function, and reduced body pain (198-201). Reduction in mental health symptoms including depression and anxiety (202, 203), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (204-208). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (209-213). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (213-216). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (217-220). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (217, 218). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 197, 221, 222). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (221, 222).	

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Nutrition intervention overall ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Dietary approaches with no specific daily energy intake goal** ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Nutrition intervention with a daily energy intake goal** ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Nutrition interventions with a daily energy intake goal followed by dietary approaches**	<u>Evidence from meta-analyses:</u> No evidence was found in this population. <u>Additional undesirable effects:</u> A reported adverse outcome of nutrition interventions was increased fasting plasma glucose with low GI diets (195). <u>Lived experience:</u> Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (197, 211, 217). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (217, 218). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (222). Fears of embarrassment and failure during exercise activities were also reported (197, 215, 222, 224). Cultural and social expectations related to food and alcohol impacted adherence (211, 215, 225). Limited access to culturally appropriate and healthy foods (215), financial constraints (226), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (214, 221, 227-229).	In addition to intentional adiposity loss, some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss. When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating.

with no specific daily energy intake goal ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know		
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Nutrition intervention overall ● Very low ○ Low ○ Moderate ○ High ○ No included studies **Dietary approaches with no specific daily energy intake goal** ○ Very low ○ Low ● Moderate ○ High ○ No included studies **Nutrition interventions with a daily energy intake goal** ○ Very low ● Low ○ Moderate ○ High ○ No included studies **Nutrition interventions with a daily energy intake goal diet followed by dietary approaches with no specific daily energy intake goal** ● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from meta-analyses:</u> The evidence is very uncertain about the effect of nutrition interventions on adiposity. <u>Evidence from meta-analyses:</u> Dietary approaches with no specific daily energy intake goal likely results in little to no difference in adiposity. <u>Evidence from narrative synthesis:</u> Dietary approaches with no specific daily energy intake goal may reduce adiposity slightly. <u>Evidence from meta-analyses:</u> Nutrition interventions with a daily energy intake goal may result in a large reduction in adiposity. <u>Evidence from meta-analyses:</u> The evidence is very uncertain about the effect of nutrition interventions with a daily energy intake goal followed by ab libitum nutrition interventions on adiposity.	
Values		

Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving nutrition treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Nutrition intervention overall ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.
Dietary approaches with no specific daily energy intake goal ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours dietary approaches with no specific daily energy intake goal interventions.	
Nutrition interventions with a daily energy intake goal	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects favours nutrition interventions with a daily energy intake goal.	

o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours the intervention ● Favours the intervention o Varies o Don't know **Nutrition interventions with a daily energy intake goal followed by dietary approaches with no specific daily energy intake goal** o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favours the intervention o Varies o Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours nutrition interventions with a daily energy intake goal followed by dietary approaches with no specific daily energy intake goal.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Nutrition interventions are not necessarily widely available and affordable.	Dietitians are expensive via the private system, and patients may experience a lack of access through the public health system. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ No included studies	Two systematic reviews on the cost-effectiveness of commercially available weight loss interventions were identified (230, 231). In the more recent of these reviews (230), the reviewers concluded that Jenny Craig was neither cost-effective (i.e., good value for money) nor cost saving (i.e., a positive return on investment). There was evidence that both Weight Watchers and Optifast were cost-effective and cost saving, but methodological issues were identified that raised doubts about the claims of cost savings.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and/or unaffordable for disadvantaged or remote populations. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with

		a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving nutrition treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where nutrition is individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of nutrition interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	**Moderate**	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	**Low**	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	**Strong recommendation for the intervention**
○	○	○	●	●

CONCLUSIONS

Recommendation

Nutrition interventions with a daily energy intake goal and/or dietary approaches with no specific daily energy intake goal:
Consensus statement due to very low certainty of evidence:
Nutrition interventions with a daily energy intake goal and/or dietary approaches with no specific daily energy intake goal may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

Dietary approaches with no specific daily energy intake goal:
Strong recommendation for the intervention:
Dietary approaches with no specific daily energy intake goal should be recommended as part of a comprehensive approach for the management of weight-related health and wellbeing.

Nutrition interventions with a daily energy intake goal:
Conditional recommendation for the intervention:
Nutrition interventions with a daily energy intake goal may be recommended as part of a comprehensive approach for the management of weight-related health and wellbeing.

Nutrition interventions with a daily energy intake goal followed by dietary approaches with no specific daily energy intake goal:
Consensus statement due to very low certainty of evidence:
Nutrition interventions with a daily energy intake goal, followed by dietary approaches with no specific daily energy intake goal may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064

11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, et al. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, et al. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, et al. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010

31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, et al. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatology International. 2020;14(2):259-69. doi: https://dx.doi.org/10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clinics and Research in Hepatology and Gastroenterology. 2021;45(4):101526. doi: https://dx.doi.org/10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, et al. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Digestive Diseases. 2022;40(6):734-44. doi: https://dx.doi.org/10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248

53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: https://dx.doi.org/10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: https://dx.doi.org/10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, et al. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: https://doi.org/10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Annals of Oncology. 2019;30(4):528-41. doi: https://dx.doi.org/10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. European Journal of Cancer. 2011;47(11):1606-15. doi: https://dx.doi.org/10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525

76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, et al. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, et al. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers. 2023;15(10):2778. doi: https://doi.org/10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, et al. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, et al. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. European Journal of Cancer. 2023;185:150-63. doi: https://doi.org/10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, et al. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, et al. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: https://dx.doi.org/10.1371/journal.pone.0053916

99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. European Journal of Epidemiology. 2023;38:135–44. doi: https://doi.org/10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, et al. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: https://dx.doi.org/10.1186/s13643-021-01606-8

121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, et al. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Seminars in Cancer Biology. 2023;91:70-98. doi: https://doi.org/10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, et al. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, et al. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, et al. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535

146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, et al. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. European Journal of Medical Research. 2022;27:311. doi: https://doi.org/10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Women's Health. 2023;23:392. doi: https://doi.org/10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, et al. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: https://doi.org/10.1002/oby.20107
164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. Journal of Psychiatric Research. 2023;163:86-92. doi: https://doi.org/10.1016/j.jpsychires.2023.05.034
166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018

169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, et al. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Blomster H, Laitinen T, Lyyra-Laitinen T, Vanninen E, Gylling H, Peltonen M, et al. Endothelial function is well preserved in obese patients with mild obstructive sleep apnea. Sleep Breath. 2014;18(1):177-86. doi: https://dx.doi.org/10.1007/s11325-013-0867-7
178. Brown JC, Sarwer DB, Troxel AB, Sturgeon K, DeMichele AM, Denlinger CS, et al. A randomized trial of exercise and diet on body composition in survivors of breast cancer with overweight or obesity. Breast Cancer Res Treat. 2021;189(1):145-54. doi: https://dx.doi.org/10.1007/s10549-021-06284-7
179. Christensen P, Frederiksen R, Bliddal H, Riecke BF, Bartels EM, Henriksen M, et al. Comparison of three weight maintenance programs on cardiovascular risk, bone and vitamins in sedentary older adults. Obesity. 2013;21(10):1982-90. doi: 10.1002/oby.20413
180. Fontana L, Villareal DT, Das SK, Smith SR, Meydani SN, Pittas AG, et al. Effects of 2-year calorie restriction on circulating levels of IGF-1, IGF-binding proteins and cortisol in nonobese men and women: a randomized clinical trial. Aging Cell. 2016;15(1):22-7. doi: https://dx.doi.org/10.1111/acel.12400
181. Foster-Schubert KE, Alfano CM, Duggan CR, Xiao L, Campbell KL, Kong A, et al. Effect of diet and exercise, alone or combined, on weight and body composition in overweight-to-obese postmenopausal women. Obesity. 2012;20(8):1628-38. doi: https://dx.doi.org/10.1038/oby.2011.76
182. Georgoulis M, Yiannakouris N, Kechribari I, Lamprou K, Perraki E, Vagiakis E, et al. Sustained improvements in the cardiometabolic profile of patients with obstructive sleep apnea after a weight-loss Mediterranean diet/lifestyle intervention: 12-month follow-up (6 months post-intervention) of the "MIMOSA" randomized clinical trial. Nutr Metab Cardiovasc Dis. 2023;33(5):1019-28. doi: https://doi.org/10.1016/j.numecd.2023.02.010
183. Hajek P, Przulj D, Pesola F, McRobbie H, Peerbux S, Phillips-Waller A, et al. A randomised controlled trial of the 5:2 diet. PLoS ONE. 2021;16(11):e0258853. doi: https://dx.doi.org/10.1371/journal.pone.0258853
184. Hershey MS, Chang C-R, Sotos-Prieto M, Fernandez-Montero A, Cash SB, Christophi CA, et al. Effect of a nutrition intervention on mediterranean diet adherence among firefighters: a cluster randomized clinical trial. JAMA Netw Open. 2023;6(8):e2329147. doi: 10.1001/jamanetworkopen.2023.29147
185. Lin S, Cienfuegos S, Ezpeleta M, Pavlou V, Chakos K, McStay M, et al. Effect of time-restricted eating versus daily calorie restriction on mood and quality of life in adults with obesity. Nutrients. 2023;15(20):4313. doi: https://doi.org/10.3390/nu15204313
186. Metzgar CJ, Nickols-Richardson SM. Effects of nutrition education on weight gain prevention: a randomized controlled trial. Nutr J. 2016;15:31. doi: 10.1186/s12937-016-0150-4
187. Montemayor S, Bouzas C, Mascaró CM, Casares M, Llompart I, Abete I, et al. Effect of dietary and lifestyle interventions on the amelioration of NAFLD in patients with metabolic syndrome: the FLIPAN study. Nutrients. 2022;14(11):2223. doi: 10.3390/nu14112223
188. Murphy JC, McDaniel JL, Mora K, Villareal DT, Fontana L, Weiss EP. Preferential reductions in intermuscular and visceral adipose tissue with exercise-induced weight loss compared with calorie restriction. J Appl Physiol (1985). 2012;112(1):79-85. doi: https://dx.doi.org/10.1152/japplphysiol.00355.2011

189. Perry CD, Degeneffe D, Davey C, Kollannoor-Samuel G, Reicks M. Weight gain prevention among midlife women: a randomized controlled trial to address needs related to the physical and social environment. Int J Environ Res Public Health. 2016;13(6):530. doi: https://dx.doi.org/10.3390/ijerph13060530
190. Pimentel GD, Portero-McLellan KC, Oliveira ÉP, Spada APM, Oshiiwa M, Zemdegs JCS, et al. Long-term nutrition education reduces several risk factors for type 2 diabetes mellitus in Brazilians with impaired glucose tolerance. Nutr Res. 2010;30(3):186-90. doi: https://dx.doi.org/10.1016/j.nutres.2010.03.003
191. Yin X, Yan L, Lu Y, Jiang Q, Pu Y, Sun Q. Correction of hypovitaminosis D does not improve the metabolic syndrome risk profile in a Chinese population: a randomized controlled trial for 1 year. Asia Pac J Clin Nutr. 2016;25(1):71-7. doi: https://dx.doi.org/10.6133/apjcn.2016.25.1.06
192. Yin Z, Perry J, Duan X, He M, Johnson R, Feng Y, et al. Cultural adaptation of an evidence-based lifestyle intervention for diabetes prevention in Chinese women at risk for diabetes: results of a randomized trial. Int Health. 2018;10(5):391-400. doi: https://dx.doi.org/10.1093/inthealth/ihx072
193. Hinderliter AL, Sherwood A, Craighead LW, Lin P-H, Watkins L, Babyak MA, et al. The long-term effects of lifestyle change on blood pressure: one-year follow-up of the ENCORE study. Am J Hypertens. 2014;27(5):734-41. doi: https://dx.doi.org/10.1093/ajh/hpt183
194. Huang YS, Zheng Q, Yang H, Fu X, Zhang X, Xia C, et al. Efficacy of intermittent or continuous very low-energy diets in overweight and obese individuals with type 2 diabetes mellitus: a systematic review and meta-analyses. J Diabetes Res. 2020;2020:4851671. doi: https://dx.doi.org/10.1155/2020/4851671
195. Schwingshackl L, Hoffmann G. Long-term effects of low glycemic index/load vs. high glycemic index/load diets on parameters of obesity and obesity-associated risks: a systematic review and meta-analysis. Nutr Metab Cardiovasc Dis. 2013;23(8):699-706. doi: https://dx.doi.org/10.1016/j.numecd.2013.04.008
196. Atallah R, Filion KB, Wakil SM, Genest J, Joseph L, Poirier P, et al. Long-term effects of 4 popular diets on weight loss and cardiovascular risk factors: a systematic review of randomized controlled trials. Circ Cardiovasc Qual Outcomes. 2014;7(6):815-27. doi: https://dx.doi.org/10.1161/CIRCOUTCOMES.113.000723
197. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
198. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: https://doi.org/10.1371/journal.pone.0119017
199. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: https://doi.org/10.1111/obr.13317
200. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: https://doi.org/10.1111/obr.13261
201. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: https://doi.org/10.1177/10998004221099556
202. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
203. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: https://doi.org/10.1111/obr.12752
204. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
205. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: https://doi.org/10.1093/nutrit/nuz020
206. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: https://doi.org/10.1111/obr.13201

207. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
208. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: https://doi.org/10.1002/14651858.CD012650.pub2
209. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: https://doi.org/10.1016/j.eprac.2022.10.006
210. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expectations. 2018;21(3):574-84. doi: https://doi.org/10.1111/hex.12667
211. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: https://doi.org/10.1111/obr.13398
212. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expectations. 2018;21(3):563-73. doi: https://doi.org/10.1111/hex.12657
213. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: https://doi.org/10.3390/nu15051297
214. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: https://doi.org/10.3310/hta22680
215. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
216. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. International Journal of Qualitative Studies on Health and Well-being. 2021;16(1):1862481. doi: https://doi.org/10.1080/17482631.2020.1862481
217. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychology Review. 2017;11(2):145-63. doi: https://doi.org/10.1080/17437199.2017.1299583
218. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: https://doi.org/10.1111/obr.12500
219. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: https://doi.org/10.1111/aphw.12132
220. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qualitative Health Research. 2019;29(1):124-34. doi: https://doi.org/10.1177/1049732318784815
221. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
222. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. International Journal of Qualitative Studies on Health and Well-being. 2015;10(1):28577. doi: https://doi.org/10.3402/qhw.v10.28577
223. Halle M, Röhling M, Banzer W, Braumann KM, Kempf K, McCarthy D, et al. Meal replacement by formula diet reduces weight more than a lifestyle intervention alone in patients with overweight or obesity and accompanied cardiovascular risk factors-the ACOORH trial. Eur J Clin Nutr. 2021;75(4):661-9. doi: https://dx.doi.org/10.1038/s41430-020-00783-4
224. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: https://doi.org/10.1371/journal.pone.0253114
225. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: https://doi.org/10.1002/oby.23743
226. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: https://doi.org/10.1111/obr.13355

227. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: https://doi.org/10.1111/cob.12347
228. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expectations. 2013;16(2):119-42. doi: https://doi.org/10.1111/j.1369-7625.2011.00699.x
229. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227
230. Finkelstein EA, Chodavadia PA, Strombotne K. A systematic review of the economic value proposition for commercially available nonsurgical weight-loss interventions. Obesity (Silver Spring). 2023;31(7):1725-33. doi: 10.1002/oby.23760
231. Finkelstein EA, Kruger E. Meta- and cost-effectiveness analysis of commercial weight loss strategies. Obesity (Silver Spring). 2014;22(9):1942-51. doi: 10.1002/oby.20824

Question: Nutrition interventions compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	nutrition interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Nutrition intervention vs untreated comparator (baseline to 12 months) - meta-analysis												
15[a]	randomised trials	serious[b]	very serious[c]	not serious	not serious	none	1362	1106	-	Hedges' g 0.47 **lower** (0.76 lower to 0.18 lower)	⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.
Nutrition intervention (**Dietary approaches with no specific daily energy intake goal**) vs untreated **comparator (baseline to 12 months)** - narrative synthesis												
1[d]	randomised trials	serious[e]	not serious	not serious	serious[f]	none	1/1 study found a positive effect of a nutrition intervention on weight maintenance/loss Weight reduced by 1.1 kgs in the intervention arm compared to 0.8 kgs in the comparator arm				⊕⊕◯◯ Low	A nutrition intervention may reduce adiposity slightly
Dietary approaches with no specific daily energy intake goal vs untreated comparator (baseline to 12 months) - meta-analysis												
8[g]	randomised trials	serious[h]	not serious	not serious	not serious	none	695	643	-	Hedges' g **0.16 lower** (0.3 lower to 0.03 lower)	⊕⊕⊕◯ Moderate	Dietary approaches with no specific daily energy intake goal likely results in little to no difference in adiposity
Nutrition intervention **with a daily energy goal vs untreated comparator (baseline to 12 months)** - meta-analysis												
4[i]	randomised trials	serious[j]	very serious[k]	not serious	not serious	strong association	476	268	-	Hedges' g 0.87 **lower** (1.72 lower to 0.03 lower)	⊕⊕◯◯ Low[j,]	Nutrition interventions with a daily energy goal nutrition may result in a large reduction in adiposity
Nutrition with a daily energy goal followed by dietary approaches with no specific daily energy intake goal **vs untreated comparator (baseline to 12 months)** - meta-analysis												
3[l]	randomised trials	serious[m]	serious[n]	not serious	serious[o]	none	191	195	-	Hedges' g 0.77 **lower** (1.84 lower to 0.31 higher)	⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity

CI: confidence interval

Explanations

a. 15 studies (18 intervention arms)
b. -1 using RoB-2 risk of bias was rated Low (5 (9%) outcomes), Some concerns (31 (54%) outcomes), High (21 (37%) outcomes)
c. -2 Inconsistency of I2=92.08%
d. 1 study, with 1 intervention arm
e. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
f. -1 Imprecision due to small sample size (Total n<400)
g. 8 studies, with 10 intervention arms
h. -1 using RoB-2 risk of bias was rated Some concerns (20 (59%) outcomes), High (14 (41%) outcomes)
i. 4 studies, with 5 intervention arms
j. -1 using RoB-2 risk of bias was rated Low (5 (42%) outcomes), Some concerns (5 (42%) outcomes), High (2 (16%) outcomes)
k. -2 Inconsistency of I2=96.39%
l. 3 studies with 3 interventions arms
m. -1 using RoB-2 risk of bias rated Some concerns (6 (55%) outcomes), High (5 (45%) outcomes)
n. -1 Inconsistency of I2=82.95%
o. -1 Imprecision due to 95% CI crosses 1.0 and small sample size (Total n<400)

QUESTION

Should physical activity interventions vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults experiencing overweight or obesity
INTERVENTION:	Physical activity interventions: • Physical activity intervention vs untreated comparator (baseline to 12 months) • Aerobic exercise intervention vs untreated comparator (baseline to 12 months) • Strengthening activities intervention vs untreated comparator (baseline to 12 months); • Combination of aerobic exercise and strengthening activities interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare.

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle aged adults. <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). <u>Type 2 diabetes mellitus</u>	

Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45).

<u>Non-alcoholic fatty liver disease</u>
Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52).

<u>Musculoskeletal conditions</u>
Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56).

<u>Cancer</u>
When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161).

<u>Mental health</u>
Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162).

<u>Health-related quality of life ratings</u>
Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167).

<u>Reproductive health</u>
Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174).

Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

Physical activity intervention overall: ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 11 studies (177-187) with 763 intervention participants and 607 comparator participants, evidence demonstrated a small effect of Hedges' 0.26 lower (95% CI 0.43 lower to 0.09 lower) in the physical activity interventions versus comparator. <u>Evidence from narrative synthesis:</u> 2 additional studies (188, 189) unable to be included in the meta-analysis found a positive effect of physical activity interventions on weight maintenance/loss.	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (216), Healthy China Initiative (217), Finnish Diabetes Prevention Study (218)) overwhelmingly support positive health outcomes of physical activity. In adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (219).
Aerobic exercise intervention: ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 8 studies (180-187) with 538 intervention participants and 430 comparator participants, evidence demonstrated a moderate effect of Hedges' g 0.41 lower (95% CI 0.57 lower to 0.25 lower) in aerobic exercise interventions versus comparator. <u>Evidence from narrative synthesis:</u> 1 additional study (188) unable to be included in the meta-analysis found a favourable effect of an aerobic exercise intervention on weight maintenance/loss. Weight change was -1.3 kgs in the intervention arm versus +0.1 kgs in the comparator arm.	
Strengthening activities intervention: ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 2 studies (178, 186) with 79 intervention participants and 79 comparator participants, evidence demonstrated a small effect of Hedges' g 0.18 higher (95% CI 0.1 lower to 0.47 higher) in strengthening activities interventions versus comparator.	
Combined aerobic and strengthening activities intervention: ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 4 studies (177, 179, 182, 186) with 146 intervention participants and 150 comparator participants, evidence demonstrated a trivial effect of Hedges' g 0.03 lower (95% CI 0.12 lower to 0.05 higher) in combining aerobic exercise and strengthening activities interventions versus comparator. <u>Evidence from narrative synthesis:</u> 1 additional study(189) unable to be included in the meta-analysis found a favourable effect of an intervention combining aerobic and strengthening activities on weight maintenance/loss. Weight change was -0.66 kgs in the intervention arm versus -0.34 kgs in the comparator arm. <u>Additional desirable effects:</u> Physical activity interventions reduced the risk of type 2 diabetes (42). In men, specifically, physical activity interventions increased HDL-C, and reduced triglyceride levels (190). <u>Lived experience:</u> Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (191-194). Reduction in mental health symptoms including depression and anxiety (195, 196), and eating	

	disorder problems including bulimia, binge eating, and emotional eating have been reported (197-201). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (202-206). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (206-209). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (210-213). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (210, 211). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 190, 214, 215). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (214, 215).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Physical activity intervention overall: ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Aerobic exercise intervention:** ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Strengthening activities intervention:** ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Combined aerobic and strengthening activities intervention:** ○ Trivial ○ Small	<u>Evidence from meta-analyses:</u> No evidence was found in this population. <u>Evidence from meta-analyses:</u> No evidence was found in this population. <u>Evidence from meta-analyses:</u> No evidence was found in this population. <u>Evidence from meta-analyses:</u> No evidence was found in this population.	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates increased physical activity, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to overexercising. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs

○ Moderate ○ Large ○ Varies ● Don't know	<u>Additional undesirable effects:</u> No evidence was found in this population. <u>Lived experience:</u> Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (190, 204, 210). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (210, 211). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (215). Fears of embarrassment and failure during exercise activities were also reported (190, 208, 215, 220). Cultural and social expectations related to food and alcohol impacted adherence (204, 208, 221). Limited access to culturally appropriate and healthy foods (208), financial constraints (222), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (207, 214, 223-225).	to be considered during program development.

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table.	
Physical activity intervention overall: ● Very low ● Low ○ Moderate ○ High ○ No included studies	<u>Evidence from meta-analyses:</u> Physical activity interventions may reduce adiposity slightly. <u>Evidence from narrative synthesis:</u> The evidence is very uncertain about the effect of physical activity interventions on adiposity.	
Aerobic exercise intervention: ○ Very low ● Low ○ Moderate ● High ○ No included studies	<u>Evidence from meta-analyses:</u> Aerobic exercise results in a slight reduction in adiposity. <u>Evidence from narrative synthesis:</u> Aerobic exercise may reduce adiposity slightly.	
Strengthening activities intervention: ● Very low ○ Low ○ Moderate	<u>Evidence from meta-analyses:</u> The evidence is very uncertain about the effect of strengthening activities on adiposity.	

o High o No included studies **Combined aerobic and strengthening activities intervention:** ● Very low ● Low o Moderate o High o No included studies	<u>Evidence from meta-analyses:</u> Combining aerobic exercise and strengthening activities may result in little to no difference in adiposity. <u>Evidence from narrative synthesis:</u> The evidence is very uncertain about the effect of combining aerobic exercise and strengthening activities interventions on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Important uncertainty or variability o Possibly important uncertainty or variability ● Probably no important uncertainty or variability o No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving physical activity treatment. However, the committee believes that since there are benefits this treatment should be considered for all patients where clinically appropriate.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Physical activity intervention overall: o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favours the intervention o Varies o Don't know **Aerobic exercise intervention:** o Favours the comparison o Probably favours the comparison	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention. Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know		
Strengthening activities intervention: ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	
Combined aerobic and strengthening activities intervention: ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings	We have not sourced literature on the resources required for this intervention. Physical activity interventions are not necessarily widely available and affordable.	Participants reported financial barriers to structured physical activity, including expensive gym

○ Large savings ○ Varies ● Don't know	Costs of gym memberships, club fees and equipment are often borne by participants.	memberships, equipment, and clothing. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	High costs of gym memberships, club fees, and equipment are borne by participants, and may be

○ Increased ● Varies ○ Don't know		prohibitive for some people, decreasing health equity. Equity could be addressed by raising the patient's awareness of available treatments and avenues for access. For example: highlighting locally available, low-cost physical activity programs; or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e.: gap payments) when accessing the prescribed treatment; etc. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability of the intervention increases where physical activity is individually tailored and appropriate.

		Mental health should be considered and monitored.

Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of physical activity interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	**Small**	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	**Low**	Moderate	**High**			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	**Strong recommendation for the intervention**
○	○	○	●	●

CONCLUSIONS

Recommendation

Aerobic and/or strengthening activities interventions:
<u>Conditional recommendation for the intervention:</u>
Aerobic and/or strengthening activity interventions may be recommended as part of a comprehensive approach to management of weight-related health and wellbeing.

Aerobic exercise interventions:
<u>Strong recommendation for the intervention:</u>
Aerobic exercise interventions should be recommended as part of a comprehensive approach to management of weight-related health and wellbeing.

Strengthening activities interventions:
<u>Consensus statement due to limited evidence and very low certainty of evidence:</u>
Strengthening activity interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

Combined aerobic and strengthening activities interventions:
<u>Conditional recommendation for the intervention:</u>
Aerobic and strengthening activity interventions may be recommended as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948

13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, et al. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, et al. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, et al. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, et al. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3

34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatology International. 2020;14(2):259-69. doi: https://dx.doi.org/10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clinics and Research in Hepatology and Gastroenterology. 2021;45(4):101526. doi: https://dx.doi.org/10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, et al. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Digestive Diseases. 2022;40(6):734-44. doi: https://dx.doi.org/10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: https://dx.doi.org/10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: https://dx.doi.org/10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553

58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, et al. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: https://doi.org/10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Annals of Oncology. 2019;30(4):528-41. doi: https://dx.doi.org/10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. European Journal of Cancer. 2011;47(11):1606-15. doi: https://dx.doi.org/10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, et al. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, et al. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers. 2023;15(10):2778. doi: https://doi.org/10.3390/cancers15102778

82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, et al. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, et al. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. European Journal of Cancer. 2023;185:150-63. doi: https://doi.org/10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, et al. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, et al. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: https://dx.doi.org/10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232

106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. European Journal of Epidemiology. 2023;38:135–44. doi: https://doi.org/10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, et al. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: https://dx.doi.org/10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, et al. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Seminars in Cancer Biology. 2023;91:70-98. doi: https://doi.org/10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017

130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, et al. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, et al. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, et al. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, et al. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. European Journal of Medical Research. 2022;27:311. doi: https://doi.org/10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z

154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Women's Health. 2023;23:392. doi: https://doi.org/10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, et al. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: https://doi.org/10.1002/oby.20107
164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. Journal of Psychiatric Research. 2023;163:86-92. doi: https://doi.org/10.1016/j.jpsychires.2023.05.034
166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, et al. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7

177. Brown JC, Sarwer DB, Troxel AB, Sturgeon K, DeMichele AM, Denlinger CS, et al. A randomized trial of exercise and diet on body composition in survivors of breast cancer with overweight or obesity. Breast Cancer Res Treat. 2021;189(1):145-54. doi: https://dx.doi.org/10.1007/s10549-021-06284-7
178. Christensen P, Frederiksen R, Bliddal H, Riecke BF, Bartels EM, Henriksen M, et al. Comparison of three weight maintenance programs on cardiovascular risk, bone and vitamins in sedentary older adults. Obesity. 2013;21(10):1982-90. doi: 10.1002/oby.20413
179. Coleman KJ, Caparosa SL, Nichols JF, Fujioka K, Koebnick C, McCloskey KN, et al. Understanding the capacity for exercise in post-bariatric patients. Obes Surg. 2017;27(1):51-8. doi: https://dx.doi.org/10.1007/s11695-016-2240-y
180. Foster-Schubert KE, Alfano CM, Duggan CR, Xiao L, Campbell KL, Kong A, et al. Effect of diet and exercise, alone or combined, on weight and body composition in overweight-to-obese postmenopausal women. Obesity. 2012;20(8):1628-38. doi: https://dx.doi.org/10.1038/oby.2011.76
181. Friedenreich CM, Woolcott CG, McTiernan A, Terry T, Brant R, Ballard-Barbash R, et al. Adiposity changes after a 1-year aerobic exercise intervention among postmenopausal women: a randomized controlled trial. Int J Obes. 2011;35(3):427-35. doi: 10.1038/ijo.2010.147
182. Gram B, Christensen R, Christiansen C, Gram J. Effects of nordic walking and exercise in type 2 diabetes mellitus: a randomized controlled trial. Clin J Sport Med. 2010;20(5):355-61. doi: 10.1227/NEU.0b013e3181e56e0a
183. Lundgren JR, Janus C, Jensen SBK, Juhl CR, Olsen LM, Christensen RM, et al. Healthy weight loss maintenance with exercise, liraglutide, or both combined. N Engl J Med. 2021;384(18):1719-30. doi: 10.1056/NEJMoa2028198
184. Morales-Palomo F, Ramirez-Jimenez M, Ortega JF, Mora-Rodriguez R. Exercise periodization over the year improves metabolic syndrome and medication use. Med Sci Sports Exerc. 2018;50(10):1983-91. doi: https://dx.doi.org/10.1249/MSS.0000000000001659
185. Murphy JC, McDaniel JL, Mora K, Villareal DT, Fontana L, Weiss EP. Preferential reductions in intermuscular and visceral adipose tissue with exercise-induced weight loss compared with calorie restriction. J Appl Physiol (1985). 2012;112(1):79-85. doi: https://dx.doi.org/10.1152/japplphysiol.00355.2011
186. Yavari A, Najafipoor F, Aliasgarzadeh A, Niafar M, Mobasseri M. Effect of aerobic exercise, resistance training or combined training on glycaemic control and cardiovascular risk factors in patients with type 2 diabetes. Biol Sport. 2012;29(2):135-43.
187. Zhang H-J, He J, Pan L-L, Ma Z-M, Han C-K, Chen C-S, et al. Effects of moderate and vigorous exercise on nonalcoholic fatty liver disease: a randomized clinical trial. JAMA Intern Med. 2016;176(8):1074-82. doi: https://dx.doi.org/10.1001/jamainternmed.2016.3202
188. Campbell PT, Gross MD, Potter JD, Schmitz KH, Duggan C, McTiernan A, et al. Effect of exercise on oxidative stress: a 12-month randomized, controlled trial. Med Sci Sports Exerc. 2010;42(8):1448-53. doi: 10.1249/MSS.0b013e3181cfc908
189. van Gemert WA, Monninkhof EM, May AM, Peeters PH, Schuit AJ. Effect of exercise on insulin sensitivity in healthy postmenopausal women: the SHAPE study. Cancer Epidemiol Biomarkers Prev. 2015;24(1):81-7. doi: https://dx.doi.org/10.1158/1055-9965.EPI-14-0722
190. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
191. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: https://doi.org/10.1371/journal.pone.0119017
192. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: https://doi.org/10.1111/obr.13317
193. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: https://doi.org/10.1111/obr.13261
194. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: https://doi.org/10.1177/10998004221099556
195. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
196. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: https://doi.org/10.1111/obr.12752
197. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6

198. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: https://doi.org/10.1093/nutrit/nuz020
199. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: https://doi.org/10.1111/obr.13201
200. Palavras MA, Hay P, Filho CADS, Claudino A. The fficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
201. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: https://doi.org/10.1002/14651858.CD012650.pub2
202. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: https://doi.org/10.1016/j.eprac.2022.10.006
203. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expectations. 2018;21(3):574-84. doi: https://doi.org/10.1111/hex.12667
204. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: https://doi.org/10.1111/obr.13398
205. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expectations. 2018;21(3):563-73. doi: https://doi.org/10.1111/hex.12657
206. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: https://doi.org/10.3390/nu15051297
207. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: https://doi.org/10.3310/hta22680
208. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
209. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. International Journal of Qualitative Studies on Health and Well-being. 2021;16(1):1862481. doi: https://doi.org/10.1080/17482631.2020.1862481
210. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychology Review. 2017;11(2):145-63. doi: https://doi.org/10.1080/17437199.2017.1299583
211. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: https://doi.org/10.1111/obr.12500
212. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: https://doi.org/10.1111/aphw.12132
213. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qualitative Health Research. 2019;29(1):124-34. doi: https://doi.org/10.1177/1049732318784815
214. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
215. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. International Journal of Qualitative Studies on Health and Well-being. 2015;10(1):28577. doi: https://doi.org/10.3402/qhw.v10.28577
216. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
217. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
218. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230

219. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
220. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: https://doi.org/10.1371/journal.pone.0253114
221. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: https://doi.org/10.1002/oby.23743
222. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: https://doi.org/10.1111/obr.13355
223. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: https://doi.org/10.1111/cob.12347
224. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expectations. 2013;16(2):119-42. doi: https://doi.org/10.1111/j.1369-7625.2011.00699.x
225. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Physical activity interventions compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	physical activity interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Physical activity intervention vs untreated comparator (baseline to 12 months) – Meta analysis												
11[a]	randomised trials	serious[b]	serious[c]	not serious	not serious	none	763	607	-	Hedges' 0.26 **lower** (0.43 lower to 0.09 lower)	⊕⊕◯◯ Low	Physical activity interventions may reduce adiposity slightly
Physical activity intervention vs untreated comparator (baseline to 12 months) – Narrative synthesis												
2[d]	randomised trials	very serious[e]	serious[f]	not serious	serious[g]	none	2/2 studies found a positive effect of physical activity interventions on weight maintenance/loss				⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity
Aerobic exercise intervention vs untreated comparator (baseline to 12 months) – Meta analysis												
8[h]	randomised trials	not serious	not serious	not serious	not serious	none	538	430	-	Hedges' g 0.41 **lower** (0.57 lower to 0.25 lower)	⊕⊕⊕⊕ High	Aerobic exercise results in a slight reduction in adiposity
Aerobic exercise intervention vs untreated comparator (baseline to 12 months) – Narrative synthesis												
1[i]	randomised trials	serious[j]	not serious	not serious	serious[g]	none	1/1 study found a favourable effect of an aerobic exercise intervention on weight maintenance/loss Weight change was -1.3 kgs in the intervention arm versus +0.1 kgs in the comparator arm				⊕⊕◯◯ Low	Aerobic exercise may reduce adiposity slightly
Strengthening exercise intervention vs untreated comparator (baseline to 12 months) – Meta analysis												
2[d]	randomised trials	very serious[k]	not serious	not serious	serious[l]	none	79	79	-	Hedges' g 0.18 **higher** (0.1 lower to 0.47 higher)	⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity
Combination of aerobic exercise and strengthening exercise interventions vs untreated comparator (baseline to 12 months) – Meta analysis												
4[m]	randomised trials	serious[n]	not serious	not serious	serious[l]	none	146	150	-	Hedges' g 0.03 **lower** (0.12 lower to 0.05 higher)	⊕⊕◯◯ Low	Combining aerobic exercise and strengthening activities may result in little to no difference in adiposity
Combination of aerobic exercise and strengthening exercise interventions vs untreated comparator (baseline to 12 months) – Narrative synthesis												
1[i]	randomised trials	very serious[k]	not serious	not serious	serious[g]	none	1/1 study found a favourable effect of an intervention combining aerobic and strengthening exercises on weight maintenance/loss Weight change was -0.66 kgs in the intervention arm versus -0.34 kgs in the comparator arm				⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity

CI: confidence interval

Explanations

a. 11 studies, with 15 intervention arms
b. -1 using RoB-2 risk of bias rated Low (20 (42%) outcomes), Some concerns (17 (35%) outcomes) and High (11 (23%) outcomes)
c. -1 Inconsistency of I2=57.16%
d. 2 studies, with 2 intervention arms
e. -2 using RoB-2 risk of bias rate Some concerns (1 (50%) outcome) and High (1 (50%) outcome)
f. -1 due to unspecified heterogeneity due to differences in exposure
g. -1 Imprecision due to small sample size (Total n<400)
h. 8 studies, with 9 intervention arms
i. 1 study, with 1 intervention arm

j. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
k. -2 using RoB-2 risk of bias all outcomes rated High
l. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)
m. 4 studies, with 4 intervention arms
n. -1 using RoB-2 risk of bias rated Some concerns (9 (82%) outcomes) and High (2 (18%) outcomes)

QUESTION

Should interventions combining nutrition and physical activity with or without sedentary behaviour interventions vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Combined nutrition and physical activity interventions, with or without sedentary behaviour interventions: • Combined nutrition and physical activity with or without sedentary behaviour interventions vs untreated comparator (baseline to 12 months) • Combined nutrition and physical activity interventions vs untreated comparator (baseline to 12 months) • Combined nutrition and physical activity with sedentary behaviour interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25).	

Type 2 diabetes mellitus
Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45).

Non-alcoholic fatty liver disease
Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52).

Musculoskeletal conditions
Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56).

Cancer
When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age

	and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Combined nutrition and physical activity (with or without sedentary behaviour): ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Evidence from meta-analysis: From 74 studies (177-250) with 13,298 intervention participants and 10,747 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.35 lower (0.42 lower to 0.27 lower) in the combined nutrition and physical activity with or without sedentary behaviour interventions versus an untreated comparator.	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (284), Healthy China Initiative (285), Finnish Diabetes Prevention Study (286)) overwhelmingly support positive health outcomes of physical activity and
Combined nutrition and physical activity without sedentary behaviour: ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Evidence from meta-analysis: From 72 studies with 12,871 intervention participants and 10,300 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.35 lower (0.43 lower to 0.27 lower) in the combined nutrition and physical activity without sedentary behaviour interventions versus an untreated comparator.	The benefits of weight loss or maintenance on cardiometabolic outcomes were also considered when making judgement. In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (287). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (287).
Combined nutrition, physical activity, and sedentary behaviour: ○ Trivial ● Small ● Moderate ○ Large ○ Varies ○ Don't know	Evidence from meta-analysis: From 2 studies(180, 233) with 427 intervention participants and 447 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.31 lower (0.61 lower to 0.02 lower) in the combined nutrition, and physical activity, and sedentary behaviour interventions versus an untreated comparator. Additional desirable effects: Nutrition and physical activity interventions combined, showed favourable effects for cardiovascular events (251), type 2 diabetes risk (252), cancer risk (251), mental health (253), mortality (all cause, cardiovascular, and cancer mortality) (251), systolic (254, 255) and diastolic (255) blood pressure, fasting glucose (254), HbA1c levels (255, 256), and triglycerides (255). Women participating in combined nutrition and physical activity interventions had reduced incidence of type 2 diabetes and reduced systolic blood pressure (257). Additional desirable effects experienced by South Asians participating in combined nutrition and physical activity interventions included reduced diabetes incidence and reduced 2-hour glucose levels (258). Adults with prediabetes participating in combined nutrition and physical activity interventions had reduced incidence of diabetes and improved glycaemic control (259). Lived experience: Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (260-263). Reduction in mental health symptoms including depression and anxiety (253, 264), and eating	

	disorder problems including bulimia, binge eating, and emotional eating have been reported (265-269). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (270-274). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (274-277). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (278-281). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (278, 279). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 257, 282, 283). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (282, 283).	
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Combined nutrition and physical activity (with or without sedentary behaviour): ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know **Combined nutrition and physical activity without sedentary behaviour:** ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know **Combined nutrition, physical activity, and sedentary behaviour:** ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from narrative synthesis</u>: 2 of 4 additional studies unable to be included in the meta-analysis found a positive effect and 1 of 4 additional studies unable to be included in the meta-analysis found a negative effect of combining nutrition and physical activity interventions on weight maintenance/loss(288-291). 1 of 4 additional studies unable to be included in the meta-analysis found a mixed effect, with one intervention showing a positive effect and the second intervention arm a negative effect of combining nutrition and physical activity interventions on weight maintenance/loss. <u>Additional undesirable effects:</u> Decreased bone mineral density was reported as an adverse outcome experienced when undertaking a nutrition and physical activity intervention (254). <u>Lived experience</u>: Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (257, 272, 278). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (278, 279). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (283). Fears of embarrassment and failure during exercise activities were also reported (257, 276, 283, 292). Cultural and social expectations related to food and alcohol impacted adherence (272, 276, 293). Limited access to culturally appropriate and healthy foods (276), financial constraints (294), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (275, 282, 295-297).	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating and overexercising. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical

		activity programs and needs to be considered during program development.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Combined nutrition and physical activity (with or without sedentary behaviour): ● Very low ○ Low ○ Moderate ○ High ○ No included studies **Combined nutrition and physical activity without sedentary behaviour:** ● Very low ○ Low ○ Moderate ○ High ○ No included studies **Combined nutrition, physical activity, and sedentary behaviour:** ● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Evidence from meta-analysis: The evidence is very uncertain about the effect of combined nutrition and physical activity, with or without sedentary behaviour, interventions on adiposity. Evidence from narrative synthesis: The evidence is very uncertain about the effect of combined nutrition and physical activity, with or without sedentary behaviour, interventions on adiposity. Evidence from meta-analysis: The evidence is very uncertain about the effect of combined nutrition and physical activity interventions on adiposity. Evidence from narrative synthesis: The evidence is very uncertain about the effect of combined nutrition and physical activity without sedentary behaviour interventions on adiposity. Evidence from meta-analysis: The evidence is very uncertain about the effect of combined nutrition, physical activity, and sedentary behaviour interventions on adiposity.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving combined nutrition and physical activity treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may

important uncertainty or variability ○ No important uncertainty or variability		not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Combined nutrition and physical activity (with or without sedentary behaviour): ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know **Combined nutrition and physical activity without sedentary behaviour:** ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know **Combined nutrition, physical activity, and sedentary behaviour:** ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the Committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention. Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the Committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention. Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the Committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know		

Resources required
How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition and physical activity interventions are not necessarily widely available and affordable.	Dietitians expensive via private system, lack of access through public health system. Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness
Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	In a systematic review of the long-term effects and economic consequences of treatments for obesity, the modelling suggested that there were high initial costs per quality-adjusted life year (QALY) of diet and exercise, but these costs had moderated by the sixth year (298). The modelling was conservative, however, and did not incorporate potential cost savings from the reduction or resolution of other conditions, such as type 2 diabetes mellitus. In a systematic review of the cost-effectiveness of non-surgical obesity interventions in men, the reviews concluded that the evidence of the cost-effectiveness of behavioural interventions in men was highly uncertain (299). In a review of the relationship between the costs of behavioural interventions (diet and physical activity) and weight loss after 1 year in overweight adults, a 5% weight loss was associated with a cost of €110 (2007 Euros) (300). Weight reductions of at least 5% were achieved in 15 of 31 interventions, and in 8 of 9 interventions costing €300 or more. The association between cost and weight reduction diminished with increasing costs.	
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and/or unaffordable for disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. Equity could be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs; or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e.: gap payments) when accessing the prescribed treatment; etc. Social and health factors are interconnected and complex,

		with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition and physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where nutrition and physical activity programmes are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition and physical activity interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	**Varies**	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation
Combined nutrition and physical activity (with or without sedentary behaviour) interventions: Consensus statement due to very low certainty of evidence: Nutrition and physical activity (with or without sedentary behaviour) interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing. **Combined nutrition and physical activity without sedentary behaviour interventions:** Consensus statement due to very low certainty of evidence: Nutrition and physical activity without sedentary behaviour interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing. **Combined nutrition, physical activity and sedentary behaviour interventions:** Consensus statement due to very low certainty of evidence: Nutrition, physical activity, and sedentary behaviour interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004

14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, et al. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, et al. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, et al. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, et al. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623

35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatology International. 2020;14(2):259-69. doi: https://dx.doi.org/10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clinics and Research in Hepatology and Gastroenterology. 2021;45(4):101526. doi: https://dx.doi.org/10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, et al. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Digestive Diseases. 2022;40(6):734-44. doi: https://dx.doi.org/10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: https://dx.doi.org/10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: https://dx.doi.org/10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, et al. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: https://doi.org/10.1080/01635581.2023.2180824

59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Annals of Oncology. 2019;30(4):528-41. doi: https://dx.doi.org/10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. European Journal of Cancer. 2011;47(11):1606-15. doi: https://dx.doi.org/10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, et al. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, et al. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers. 2023;15(10):2778. doi: https://doi.org/10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042

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83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, et al. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, et al. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. European Journal of Cancer. 2023;185:150-63. doi: https://doi.org/10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, et al. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, et al. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: https://dx.doi.org/10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945

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107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. European Journal of Epidemiology. 2023;38:135–44. doi: https://doi.org/10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, et al. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: https://dx.doi.org/10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, et al. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Seminars in Cancer Biology. 2023;91:70-98. doi: https://doi.org/10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017

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130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, et al. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, et al. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, et al. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, et al. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. European Journal of Medical Research. 2022;27:311. doi: https://doi.org/10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z

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154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Women's Health. 2023;23:392. doi: https://doi.org/10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, et al. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: https://doi.org/10.1002/oby.20107
164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. Journal of Psychiatric Research. 2023;163:86-92. doi: https://doi.org/10.1016/j.jpsychires.2023.05.034
166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, et al. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7

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177. Ahern AL, Wheeler GM, Aveyard P, Boyland EJ, Halford JCG, Mander AP, et al. Extended and standard duration weight-loss programme referrals for adults in primary care (WRAP): a randomised controlled trial. Lancet. 2017;389(10085):2214-25. doi: 10.1016/S0140-6736(17)30647-5
178. Almeida FA, You W, Brito FA, Alves TF, Goessl C, Wall SS, et al. A randomized controlled trial to test the effectiveness of two technology-enhanced diabetes prevention programs in primary care: the DiaBEAT-it study. Front Public Health. 2023;11:1000162. doi: https://doi.org/10.3389/fpubh.2023.1000162
179. Amer OE, Sabico S, Alfawaz HA, Aljohani N, Hussain SD, Alnaami AM, et al. Reversal of prediabetes in Saudi adults: results from an 18 month lifestyle intervention. Nutrients. 2020;12(3):804. doi: https://dx.doi.org/10.3390/nu12030804
180. Andersen E, van der Ploeg HP, van Mechelen W, Gray CM, Mutrie N, van Nassau F, et al. Contributions of changes in physical activity, sedentary time, diet and body weight to changes in cardiometabolic risk. Int J Behav Nutr Phys Act. 2021;18:166. doi: https://dx.doi.org/10.1186/s12966-021-01237-1
181. Anderson AS, Chong HY, Craigie AM, Donnan PT, Gallant S, Hickman A, et al. A novel approach to increasing community capacity for weight management a volunteer-delivered programme (ActWELL) initiated within breast screening clinics: a randomised controlled trial. Int J Behav Nutr Phys Act. 2021;18:34. doi: 10.1186/s12966-021-01099-7
182. Bowen DJ, Quintiliani LM, Bhosrekar SG, Goodman R, Smith E. Changing the housing environment to reduce obesity in public housing residents: a cluster randomized trial. BMC Public Health. 2018;18:883. doi: 10.1186/s12889-018-5777-y
183. Brown JC, Sarwer DB, Troxel AB, Sturgeon K, DeMichele AM, Denlinger CS, et al. A randomized trial of exercise and diet on body composition in survivors of breast cancer with overweight or obesity. Breast Cancer Res Treat. 2021;189(1):145-54. doi: https://dx.doi.org/10.1007/s10549-021-06284-7
184. Cadmus-Bertram L, Nelson SH, Hartman S, Patterson RE, Parker BA, Pierce JP. Randomized trial of a phone- and web-based weight loss program for women at elevated breast cancer risk: the HELP study. J Behav Med. 2016;39(4):551-9. doi: https://dx.doi.org/10.1007/s10865-016-9735-9
185. Cassidy S, Trenell M, Stefanetti RJ, Charman SJ, Barnes AC, Brosnahan N, et al. Physical activity, inactivity and sleep during the Diabetes Remission Clinical Trial (DiRECT). Diabet Med. 2023;40(3):e15010. doi: https://doi.org/10.1111/dme.15010
186. Conroy MB, Sward KL, Spadaro KC, Tudorascu D, Karpov I, Jones BL, et al. Effectiveness of a physical activity and weight loss intervention for middle-aged women: healthy bodies, healthy hearts randomized trial. J Gen Intern Med. 2015;30(2):207-13. doi: 10.1007/s11606-014-3077-5
187. de Vos BC, Runhaar J, Bierma-Zeinstra SMA. Effectiveness of a tailor-made weight loss intervention in primary care. Eur J Nutr. 2014;53(1):95-104. doi: https://dx.doi.org/10.1007/s00394-013-0505-y
188. Debussche X, Rollot O, Le Pommelet C, Fianu A, Le Moullec N, Régnier C, et al. Quarterly individual outpatients lifestyle counseling after initial inpatients education on type 2 diabetes: the REDIA Prev-2 randomized controlled trial in Reunion Island. Diabetes Metab. 2012;38(1):46-53. doi: https://dx.doi.org/10.1016/j.diabet.2011.07.002
189. Demark-Wahnefried W, Jones LW, Snyder DC, Sloane RJ, Kimmick GG, Hughes DC, et al. Daughters and Mothers Against Breast Cancer (DAMES): main outcomes of a randomized controlled trial of weight loss in overweight mothers with breast cancer and their overweight daughters. Cancer. 2014;120(16):2522-34. doi: 10.1002/cncr.28761
190. Duncan MJ, Fenton S, Brown WJ, Collins CE, Glozier N, Kolt GS, et al. Efficacy of a multi-component m-health weight-loss intervention in overweight and obese adults: a randomised controlled trial. Int J Environ Res Public Health. 2020;17(17):6200. doi: https://dx.doi.org/10.3390/ijerph17176200
191. Fjeldsoe BS, Goode AD, Phongsavan P, Bauman A, Maher G, Winkler E, et al. Get Healthy, Stay Healthy: evaluation of the maintenance of lifestyle changes six months after an extended contact intervention. JMIR mHealth uHealth. 2019;7(3):e11070. doi: https://dx.doi.org/10.2196/11070
192. Foster-Schubert KE, Alfano CM, Duggan CR, Xiao L, Campbell KL, Kong A, et al. Effect of diet and exercise, alone or combined, on weight and body composition in overweight-to-obese postmenopausal women. Obesity. 2012;20(8):1628-38. doi: https://dx.doi.org/10.1038/oby.2011.76
193. Gessler N, Willems S, Steven D, Aberle J, Akbulak RO, Gosau N, et al. Supervised Obesity Reduction Trial for AF ablation patients: results from the SORT-AF trial. Europace. 2021;23(10):1548-58. doi: 10.1093/europace/euab122
194. Gilcharan Singh HK, Chee WSS, Hamdy O, Mechanick JI, Lee VKM, Barua A, et al. Eating self-efficacy changes in individuals with type 2 diabetes following a structured lifestyle intervention based on the transcultural Diabetes Nutrition Algorithm (tDNA): a secondary analysis of a randomized controlled trial. PLoS ONE. 2020;15(11):e0242487. doi: https://dx.doi.org/10.1371/journal.pone.0242487
195. Glasgow RE, Kurz D, King D, Dickman JM, Faber AJ, Halterman E, et al. Twelve-month outcomes of an Internet-based diabetes self-management support program. Patient Educ Couns. 2012;87(1):81-92. doi: https://dx.doi.org/10.1016/j.pec.2011.07.024
196. Goodwin PJ, Segal RJ, Vallis M, Ligibel JA, Pond GR, Robidoux A, et al. Randomized trial of a telephone-based weight loss intervention in postmenopausal women with breast cancer receiving letrozole: the LISA Trial. J Clin Oncol. 2014;32(21):2231-9. doi: 10.1200/JCO.2013.53.1517
197. Harvie M, Pegington M, McMullan D, Bundred N, Livingstone K, Campbell A, et al. The effectiveness of home versus community-based weight control programmes initiated soon after breast cancer diagnosis: a randomised controlled trial. Br J Canc. 2019;121:443-54. doi: https://dx.doi.org/10.1038/s41416-019-0522-6

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198. Hoerster KD, Hunter-Merrill R, Nguyen T, Rise P, Barón AE, McDowell J, et al. Effect of a remotely delivered self-directed behavioral intervention on body weight and physical health status among adults with obesity: the D-ELITE randomized clinical trial. JAMA. 2022;328(22):2230-41. doi: https://dx.doi.org/10.1001/jama.2022.21177
199. Jakicic JM, Otto AD, Lang W, Semler L, Winters C, Polzien K, et al. The effect of physical activity on 18-month weight change in overweight adults. Obesity. 2011;19(1):100-9. doi: https://dx.doi.org/10.1038/oby.2010.122
200. Jansson SP, Engfeldt P, Magnuson A, Lohse PT G, Liljegren G. Interventions for lifestyle changes to promote weight reduction, a randomized controlled trial in primary health care. BMC Res Notes. 2013;6:213. doi: https://dx.doi.org/10.1186/1756-0500-6-213
201. Janus ED, Best JD, Davis-Lameloise N, Philpot B, Hernan A, Bennett CM, et al. Scaling-up from an implementation trial to state-wide coverage: results from the preliminary Melbourne Diabetes Prevention Study. Trials. 2012;13:152. doi: https://dx.doi.org/10.1186/1745-6215-13-152
202. Jebb SA, Ahern AL, Olson AD, Aston LM, Holzapfel C, Stoll J, et al. Primary care referral to a commercial provider for weight loss treatment versus standard care: a randomised controlled trial. Lancet. 2011;378(9801):1485-92. doi: https://dx.doi.org/10.1016/S0140-6736(11)61344-5
203. Johansen MY, MacDonald CS, Hansen KB, Karstoft K, Christensen R, Pedersen M, et al. Effect of an intensive lifestyle intervention on glycemic control in patients with type 2 diabetes: a randomized clinical trial. JAMA. 2017;318(7):637-46. doi: https://dx.doi.org/10.1001/jama.2017.10169
204. Juul L, Andersen VJ, Arnoldsen J, Maindal HT. Effectiveness of a brief theory-based health promotion intervention among adults at high risk of type 2 diabetes: One-year results from a randomised trial in a community setting. Prim Care Diabetes. 2016;10(2):111-20. doi: 10.1016/j.pcd.2015.07.002
205. Kalarchian MA, Marcus MD, Courcoulas AP, Cheng Y, Levine MD, Josbeno D. Optimizing long-term weight control after bariatric surgery: a pilot study. Surg Obes Relat Dis. 2012;8(6):710-5. doi: https://dx.doi.org/10.1016/j.soard.2011.04.231
206. Katula JA, Vitolins MZ, Morgan TM, Lawlor MS, Blackwell CS, Isom SP, et al. The Healthy Living Partnerships to Prevent Diabetes study: 2-year outcomes of a randomized controlled trial. Am J Prev Med. 2013;44(4 Suppl 4):S324-S32. doi: https://dx.doi.org/10.1016/j.amepre.2012.12.015
207. Katzmarzyk PT, Martin CK, Newton RL, Jr., Apolzan JW, Arnold CL, Davis TC, et al. Weight loss in underserved patients - a cluster-randomized trial. N Engl J Med. 2020;383(10):909-18. doi: https://dx.doi.org/10.1056/NEJMoa2007448
208. Kegler MC, Haardörfer R, Alcantara IC, Gazmararian JA, Veluswamy JK, Hodge TL, et al. Impact of improving home environments on energy intake and physical activity: a randomized controlled trial. Am J Public Health. 2016;106(1):143-52. doi: 10.2105/AJPH.2015.302942
209. Kempf K, Röhling M, Martin S, Schneider M. Telemedical coaching for weight loss in overweight employees: a three-armed randomised controlled trial. BMJ Open. 2019;9(4):e022242. doi: https://dx.doi.org/10.1136/bmjopen-2018-022242
210. Kennedy BM, Ryan DH, Johnson WD, Harsha DW, Newton RL, Jr., Champagne CM, et al. Baton Rouge Healthy Eating and Lifestyle Program (BR-HELP): a pilot health promotion program. J Prev Interv Community. 2015;43(2):95-108. doi: 10.1080/10852352.2014.973256
211. López-Padrós C, Salord N, Alves C, Vilarrasa N, Gasa M, Planas R, et al. Effectiveness of an intensive weight-loss program for severe OSA in patients undergoing CPAP treatment: a randomized controlled trial. J Clin Sleep Med. 2020;16(4):503-14. doi: https://dx.doi.org/10.5664/jcsm.8252
212. Lugones-Sanchez C, Recio-Rodriguez JI, Agudo-Conde C, Repiso-Gento I, G Adalia E, Ramirez-Manent JI, et al. Long-term effectiveness of a smartphone app combined with a smart band on weight loss, physical activity, and caloric intake in a population with overweight and obesity (Evident 3 Study): randomized controlled trial. J Med Internet Res. 2022;24(2):e30416. doi: https://dx.doi.org/10.2196/30416
213. Lutes LD, Damschroder LJ, Masheb R, Kim HM, Gillon L, Holleman RG, et al. Behavioral treatment for veterans with obesity: 24-month weight outcomes from the ASPIRE-VA small changes randomized trial. J Gen Intern Med. 2017;32(Suppl 1):40-7. doi: https://dx.doi.org/10.1007/s11606-017-3987-0
214. Ma J, Strub P, Xiao L, Lavori PW, Camargo CA, Jr., Wilson SR, et al. Behavioral weight loss and physical activity intervention in obese adults with asthma. A randomized trial. Ann Am Thorac Soc. 2015;12(1):1-11. doi: https://dx.doi.org/10.1513/AnnalsATS.201406-271OC
215. Mangieri CW, Johnson RJ, Sweeney LB, Choi YU, Wood JC. Mobile health applications enhance weight loss efficacy following bariatric surgery. Obes Res Clin Pract. 2019;13(2):176-9. doi: 10.1016/j.orcp.2019.01.004
216. Marrero DG, Palmer KNB, Phillips EO, Miller-Kovach K, Foster GD, Saha CK. Comparison of commercial and self-initiated weight loss programs in people with prediabetes: a randomized control trial. Am J Public Health. 2016;106(5):949-56. doi: https://dx.doi.org/10.2105/AJPH.2015.303035
217. Miguel Soca PE, Peña Pérez I, Niño Escofet S, Cruz Torres W, Niño Peña A, Ponce De León D. [Randomised controlled trial: the role of diet and exercise in women with metabolic syndrome]. Aten Primaria. 2012;44(7):387-93. doi: https://dx.doi.org/10.1016/j.aprim.2011.07.010
218. Montemayor S, Bouzas C, Mascaró CM, Casares M, Llompart I, Abete I, et al. Effect of dietary and lifestyle interventions on the amelioration of NAFLD in patients with metabolic syndrome: the FLIPAN study. Nutrients. 2022;14(11):2223. doi: 10.3390/nu14112223

219. Morgan PJ, Lubans DR, Collins CE, Warren JM, Callister R. 12-month outcomes and process evaluation of the SHED-IT RCT: an internet-based weight loss program targeting men. Obesity. 2011;19(1):142-51. doi: https://dx.doi.org/10.1038/oby.2010.119

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220. Nakade M, Aiba N, Suda N, Morita A, Miyachi M, Sasaki S, et al. Behavioral change during weight loss program and one-year follow-up: Saku Control Obesity Program (SCOP) in Japan. Asia Pac J Clin Nutr. 2012;21(1):22-34. doi: https://search.informit.org/doi/10.3316/ielapa.004014331025523

Formatted: Font: (Default) +Body (Calibri), 10 pt

221. O'Brien MJ, Perez A, Scanlan AB, Alos VA, Whitaker RC, Foster GD, et al. PREVENT-DM comparative effectiveness trial of lifestyle intervention and metformin. Am J Prev Med. 2017;52(6):788-97. doi: https://doi.org/10.1016/j.amepre.2017.01.008

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222. Parker SM, Barr M, Stocks N, Denney-Wilson E, Zwar N, Karnon J, et al. Preventing chronic disease in overweight and obese patients with low health literacy using eHealth and teamwork in primary healthcare (HeLP-GP): a cluster randomised controlled trial. BMJ Open. 2022;12(11):e060393. doi: https://dx.doi.org/10.1136/bmjopen-2021-060393

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223. Paskett ED, Baltic RD, Young GS, Katz ML, Lesko SM, Webber KH, et al. A group randomized trial to reduce obesity among Appalachian church members: the Walk by Faith study. Cancer Epidemiol Biomarkers Prev. 2018;27(11):1289-97. doi: https://dx.doi.org/10.1158/1055-9965.EPI-17-1085

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224. Patel MS, Small DS, Harrison JD, Hilbert V, Fortunato MP, Oon AL, et al. Effect of behaviorally designed gamification with social incentives on lifestyle modification among adults with uncontrolled diabetes: a randomized clinical trial. JAMA Netw Open. 2021;4(5):e2110255. doi: 10.1001/jamanetworkopen.2021.10255

225. Patrick K, Calfas KJ, Norman GJ, Rosenberg D, Zabinski MF, Sallis JF, et al. Outcomes of a 12-month web-based intervention for overweight and obese men. Ann Behav Med. 2011;42(3):391-401. doi: https://dx.doi.org/10.1007/s12160-011-9296-7

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226. Redmon JB, Bertoni AG, Connelly S, Feeney PA, Glasser SP, Glick H, et al. Effect of the look AHEAD study intervention on medication use and related cost to treat cardiovascular disease risk factors in individuals with type 2 diabetes. Diabetes Care. 2010;33(6):1153-8. doi: https://dx.doi.org/10.2337/dc09-2090

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227. Reid RD, McDonnell LA, Riley DL, Mark AE, Mosca L, Beaton L, et al. Effect of an intervention to improve the cardiovascular health of family members of patients with coronary artery disease: a randomized trial. CMAJ. 2014;186(1):23-30. doi: 10.1503/cmaj.130550

228. Risica PM, Gans KM, Kumanyika S, Kirtania U, Lasater TM. SisterTalk: final results of a culturally tailored cable television delivered weight control program for Black women. Int J Behav Nutr Phys Act. 2013;10:141. doi: https://dx.doi.org/10.1186/1479-5868-10-141

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229. Rock CL, Flatt SW, Byers TE, Colditz GA, Demark-Wahnefried W, Ganz PA, et al. Results of the Exercise and Nutrition to Enhance Recovery and Good Health for You (ENERGY) trial: a behavioral weight loss intervention in overweight or obese breast cancer survivors. J Clin Oncol. 2015;33(28):3169-76. doi: https://dx.doi.org/10.1200/JCO.2015.61.1095

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230. Rock CL, Flatt SW, Sherwood NE, Karanja N, Pakiz B, Thomson CA. Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. JAMA. 2010;304(16):1803-10. doi: https://dx.doi.org/10.1001/jama.2010.1503

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231. Ross R, Latimer-Cheung AE, Day AG, Brennan AM, Hill JO. A small change approach to prevent long-term weight gain in adults with overweight and obesity: a randomized controlled trial. CMAJ. 2022;194(9):E324-E31. doi: https://dx.doi.org/10.1503/cmaj.211041

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232. Sahlman J, Seppä J, Herder C, Peltonen M, Peuhkurinen K, Gylling H, et al. Effect of weight loss on inflammation in patients with mild obstructive sleep apnea. Nutr Metab Cardiovasc Dis. 2012;22(7):583-90. doi: 10.1016/j.numecd.2010.10.007

233. Shapiro JR, Koro T, Doran N, Thompson S, Sallis JF, Calfas K, et al. Text4Diet: a randomized controlled study using text messaging for weight loss behaviors. Prev Med. 2012;55(5):412-7. doi: 10.1016/j.ypmed.2012.08.011

234. Silva AM, Nunes CL, Jesus F, Francisco R, Matias CN, Cardoso M, et al. Effectiveness of a lifestyle weight-loss intervention targeting inactive former elite athletes: the Champ4Life randomised controlled trial. Br J Sports Med. 2022;56(7):394-402. doi: https://dx.doi.org/10.1136/bjsports-2021-104212

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235. Slater S, Lambkin D, Schumacher T, Williams A, Baillie J. Testing the effectiveness of a novel, evidence-based weight management and lifestyle modification programme in primary care: the Healthy Weight Initiative. J Prim Health Care. 2022;14(1):64-73. doi: https://doi.org/10.1071/HC21065

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236. Stumm G, Blaik A, Kropf S, Westphal S, Hantke TK, Luley C. Long-term follow-up of the telemonitoring weight-reduction program "Active Body Control". J Diabetes Res. 2016;2016:3798729. doi: https://dx.doi.org/10.1155/2016/3798729

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237. Taheri S, Zaghloul H, Chagoury O, Elhadad S, Ahmed SH, El Khatib N, et al. Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-I): an open-label, parallel-group, randomised controlled trial. Lancet Diabetes Endocrinol. 2020;8(6):477-89. doi: https://dx.doi.org/10.1016/S2213-8587(20)30117-0

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238. Tejera C, Porca C, Rodriguez-Carnero G, Andújar P, Casanueva FF, Bellido D, et al. Reducing metabolic syndrome through a group educational intervention program in adults with obesity: IGOBE program. Nutrients. 2022;14(5):1066. doi: https://dx.doi.org/10.3390/nu14051066

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239. Thomas JG, Raynor HA, Bond DS, Luke AK, Cardoso CC, Foster GD, et al. Weight loss in Weight Watchers Online with and without an activity tracking device compared to control: a randomized trial. Obesity. 2017;25(6):1014-21. doi: https://doi.org/10.1002/oby.21846

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240. Thorndike AN, McCurley JL, Gelsomin ED, Anderson E, Chang Y, Porneala B, et al. Automated behavioral workplace intervention to prevent weight gain and improve diet: the ChooseWell 365 randomized clinical trial. JAMA Netw Open. 2021;4(6):e2112528. doi: 10.1001/jamanetworkopen.2021.12528
241. Trief PM, Fisher L, Sandberg J, Cibula DA, Dimmock J, Hessler DM, et al. Health and psychosocial outcomes of a telephonic couples behavior change intervention in patients with poorly controlled type 2 diabetes: a randomized clinical trial. Diabetes Care. 2016;39(12):2165-73. doi: https://doi.org/10.2337/dc16-0035
242. Unick JL, Lang W, Williams SE, Bond DS, Egan CM, Espeland MA, et al. Objectively-assessed physical activity and weight change in young adults: a randomized controlled trial. Int J Behav Nutr Phys Act. 2017;14:165. doi: https://dx.doi.org/10.1186/s12966-017-0620-x
243. Van Name MA, Camp AW, Magenheimer EA, Li F, Dziura JD, Montosa A, et al. Effective translation of an intensive lifestyle intervention for Hispanic women with prediabetes in a community health center setting. Diabetes Care. 2016;39(4):525-31. doi: https://dx.doi.org/10.2337/dc15-1899
244. Viester L, Verhagen EALM, Bongers PM, van der Beek AJ. Effectiveness of a worksite intervention for male construction workers on dietary and physical activity behaviors, body mass index, and health outcomes: results of a randomized controlled trial. Am J Health Promot. 2018;32(3):795-805. doi: https://doi.org/10.1177/0890117117694450
245. Walc A, Latimer-Cheung AE, Day AG, Brennan AM, Hill JO, Ross R. A small change approach on adiposity, lean mass and bone mineral density in adults with overweight and obesity: a randomized controlled trial. Clin Obes. 2023;13(4):e12587. doi: https://doi.org/10.1111/cob.12587
246. Wani K, Alfawaz H, Alnaami AM, Sabico S, Khattak MNK, Al-Attas O, et al. Effects of a 12-month intensive lifestyle monitoring program in predominantly overweight/obese Arab adults with prediabetes. Nutrients. 2020;12(2):464. doi: https://doi.org/10.3390/nu12020464
247. Watson S, Woodside JV, Ware LJ, Hunter SJ, McGrath A, Cardwell CR, et al. Effect of a web-based behavior change program on weight loss and cardiovascular risk factors in overweight and obese adults at high risk of developing cardiovascular disease: randomized controlled trial. J Med Internet Res. 2015;17(7):e177. doi: 10.2196/jmir.3828
248. Werkman A, Hulshof PJM, Stafleu A, Kremers SPJ, Kok FJ, Schouten EG, et al. Effect of an individually tailored one-year energy balance programme on body weight, body composition and lifestyle in recent retirees: a cluster randomised controlled trial. BMC Public Health. 2010;10:110. doi: https://dx.doi.org/10.1186/1471-2458-10-110
249. Wilson MG, DeJoy DM, Vandenberg R, Padilla H, Davis M. FUEL Your Life: a translation of the Diabetes Prevention Program to worksites. Am J Health Promot. 2016;30(3):188-97. doi: https://doi.org/10.4278/ajhp.130411-QUAN-169
250. Zamorano AS, Wilson EM, Liu J, Leon A, Kuroki LM, Thaker PH, et al. Text-message-based behavioral weight loss for endometrial cancer survivors with obesity: a randomized controlled trial. Gynecol Oncol. 2021;162(3):770-7. doi: https://dx.doi.org/10.1016/j.ygyno.2021.06.007
251. Ma C, Avenell A, Bolland M, Hudson J, Stewart F, Robertson C, et al. Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease, and cancer: systematic review and meta-analysis. BMJ. 2017;359:j4849. doi: https://dx.doi.org/10.1136/bmj.j4849
252. LeBlanc ES, Patnode CD, Webber EM, Redmond N, Rushkin M, O'Connor EA. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2018;320(11):1172-91. doi: https://dx.doi.org/10.1001/jama.2018.7777
253. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
254. Leblanc ES, O'Connor E, Whitlock EP, Patnode CD, Kapka T. Effectiveness of primary care-relevant treatments for obesity in adults: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2011;155(7):434-47. doi: https://dx.doi.org/10.7326/0003-4819-155-7-201110040-00006
255. Dombrowski SU, Avenell A, Sniehott FF. Behavioural interventions for obese adults with additional risk factors for morbidity: systematic review of effects on behaviour, weight and disease risk factors. Obes Facts. 2010;3(6):377-96. doi: https://dx.doi.org/10.1159/000323076
256. Johnson M, Jones R, Freeman C, Woods HB, Gillett M, Goyder E, et al. Can diabetes prevention programmes be translated effectively into real-world settings and still deliver improved outcomes? A synthesis of evidence. Diabet Med. 2013;30(1):3-15. doi: https://dx.doi.org/10.1111/dme.12018
257. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
258. Jenum AK, Brekke I, Mdala I, Muilwijk M, Ramachandran A, Kjøllesdal M, et al. Effects of dietary and physical activity interventions on the risk of type 2 diabetes in South Asians: meta-analysis of individual participant data from randomised controlled trials. Diabetologia. 2019;62(8):1337-48. doi: https://dx.doi.org/10.1007/s00125-019-4905-2
259. Kerrison G, Gillis RB, Jiwani SI, Alzahrani Q, Kok S, Harding SE, et al. The effectiveness of lifestyle adaptation for the prevention of prediabetes in adults: a systematic review. J Diabetes Res. 2017;2017:8493145. doi: https://dx.doi.org/10.1155/2017/8493145

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260. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: https://doi.org/10.1371/journal.pone.0119017
261. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: https://doi.org/10.1111/obr.13317
262. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: https://doi.org/10.1111/obr.13261
263. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: https://doi.org/10.1177/10998004221099556
264. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: https://doi.org/10.1111/obr.12752
265. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
266. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: https://doi.org/10.1093/nutrit/nuz020
267. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: https://doi.org/10.1111/obr.13201
268. Palavras MA, Hay P, Filho CADS, Claudino A. The ffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
269. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: https://doi.org/10.1002/14651858.CD012650.pub2
270. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: https://doi.org/10.1016/j.eprac.2022.10.006
271. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expectations. 2018;21(3):574-84. doi: https://doi.org/10.1111/hex.12667
272. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: https://doi.org/10.1111/obr.13398
273. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expectations. 2018;21(3):563-73. doi: https://doi.org/10.1111/hex.12657
274. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: https://doi.org/10.3390/nu15051297
275. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: https://doi.org/10.3310/hta22680
276. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
277. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. International Journal of Qualitative Studies on Health and Well-being. 2021;16(1):1862481. doi: https://doi.org/10.1080/17482631.2020.1862481
278. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychology Review. 2017;11(2):145-63. doi: https://doi.org/10.1080/17437199.2017.1299583
279. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: https://doi.org/10.1111/obr.12500

280. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: https://doi.org/10.1111/aphw.12132
281. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qualitative Health Research. 2019;29(1):124-34. doi: https://doi.org/10.1177/1049732318784815
282. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
283. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. International Journal of Qualitative Studies on Health and Well-being. 2015;10(1):28577. doi: https://doi.org/10.3402/qhw.v10.28577
284. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
285. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
286. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
287. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
288. Svetkey LP, Batch BC, Lin P-H, Intille SS, Corsino L, Tyson CC, et al. Cell phone intervention for you (CITY): a randomized, controlled trial of behavioral weight loss intervention for young adults using mobile technology. Obesity. 2015;23(11):2133-41. doi: https://dx.doi.org/10.1002/oby.21226
289. ter Bogt NCW, Milder IEJ, Bemelmans WJE, Beltman FW, Broer J, Smit AJ, et al. Changes in lifestyle habits after counselling by nurse practitioners: 1-year results of the Groningen Overweight and Lifestyle study. Public Health Nutr. 2011;14(6):995-1000. doi: 10.1017/S1368980010003708
290. Napolitano MA, Whiteley JA, Mavredes M, Tjaden AH, Simmens S, Hayman LL, et al. Effect of tailoring on weight loss among young adults receiving digital interventions: an 18 month randomized controlled trial. Transl Behav Med. 2021;11(4):970-80. doi: https://dx.doi.org/10.1093/tbm/ibab017
291. Hébert JR, Wirth M, Davis L, Davis B, Harmon BE, Hurley TG, et al. C-reactive protein levels in African Americans: a diet and lifestyle randomized community trial. Am J Prev Med. 2013;45(4):430-40. doi: 10.1016/j.amepre.2013.05.011
292. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: https://doi.org/10.1371/journal.pone.0253114
293. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: https://doi.org/10.1002/oby.23743
294. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: https://doi.org/10.1111/obr.13355
295. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: https://doi.org/10.1111/cob.12347
296. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expectations. 2013;16(2):119-42. doi: https://doi.org/10.1111/j.1369-7625.2011.00699.x
297. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227
298. Avenell A, Broom J, Brown TJ, Poobalan A, Aucott L, Stearns SC, et al. Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement. Health Technol Assess. 2004;8(21):iii-iv, 1-182. doi: 10.3310/hta8210
299. Boyers D, Avenell A, Stewart F, Robertson C, Archibald D, Douglas F, et al. A systematic review of the cost-effectiveness of non-surgical obesity interventions in men. Obes Res Clin Pract. 2015;9(4):310-27. doi: 10.1016/j.orcp.2015.03.001
300. Bogers RP, Barte JC, Schipper CM, Vijgen SM, de Hollander EL, Tariq L, et al. Relationship between costs of lifestyle interventions and weight loss in overweight adults. Obes Rev. 2010;11(1):51-61. doi: 10.1111/j.1467-789X.2009.00606.x

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Question: Interventions combining nutrition and physical activity with or without sedentary behaviour compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interventions combining nutrition and physical activity with or without sedentary behaviour	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Combined nutrition and physical activity with or without sedentary behaviour interventions vs untreated comparator (baseline to 12 months) – Meta-**analysis**												
74[a]	randomised trials	serious[b]	very serious[c]	not serious	not serious	none	13298	10747	-	Hedges' g 0.35 **lower** (0.42 lower to 0.27 lower)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.
Combined nutrition and physical activity interventions vs untreated comparator (baseline to 12 months) – Meta-**analysis**												
72[g]	randomised trials	serious[h]	very serious[i]	not serious	not serious	none	12871	10300	-	Hedges' g 0.35 **lower** (0.43 lower to 0.27 lower)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.
Combined nutrition and physical activity interventions vs untreated comparator (baseline to 12 months) – Narrative synthesis												
4[d]	randomised trials	very serious[e]	serious[f]	not serious	not serious	none	2/4 studies found a positive effect and 1/4 studies found a negative effect of combining nutrition and physical activity interventions on weight maintenance/loss. 1 further study found a mixed effect, with one intervention showing a positive effect and the second intervention arm a negative effect of combining nutrition and physical activity interventions on weight maintenance/loss				⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.
Combined nutrition and physical activity with sedentary behaviour interventions vs untreated comparator (baseline to 12 months) – Meta-**analysis**												
2[j]	randomised trials	very serious[k]	serious[l]	not serious	not serious	none	427	447	-	Hedges' g 0.31 **lower** (0.61 lower to 0.02 lower)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 74 studies, with 88 intervention arms
b. -1 using RoB-2 risk of bias rated Low (32 (15%) outcomes), Some concerns (108 (50%) outcomes), High (75 (35%) outcomes)
c. -2 Inconsistency of I2=87.43%
d. 4 studies, with 5 intervention arms
e. -2 using RoB-2 risk of bias rated Some concerns (1 (20%) outcome), High (4 (80%) outcomes)
f. -1 due to unspecified heterogeneity due to differences in exposure
g. 72 studies, with 86 intervention arms.
h. -1 using RoB-2 risk of bias rated Low (32 (15%), Some concerns (107 (50%) outcomes), High (73 (35%) outcomes)
i. Downgrade by 2 as I2 = 87.55%
j. 2 studies, with 2 intervention arms
k. -2 using RoB-2 risk of bias rated Some concerns (1 (33%) outcome), High (2 (67%) outcomes)
l. -1 Inconsistency of I2=68.99%

QUESTION

Should interventions combining nutrition, physical activity and psychological vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and psychological interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). <u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a	

healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45).

<u>Non-alcoholic fatty liver disease</u>
Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52).

<u>Musculoskeletal conditions</u>
Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56).

<u>Cancer</u>
When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132).

	Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 21 studies (177-197) with 4201 intervention participants and 1904 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.45 lower (95%CI 0.68 lower to 0.23 lower) in nutrition, physical activity, and psychological interventions versus untreated comparator. <u>Evidence from narrative synthesis:</u> 4 additional studies (198-201) unable to be included in the meta-analysis found a positive effect for combining nutrition, physical activity, and psychological interventions on weight maintenance/loss. <u>Additional desirable effects:</u> In men only, nutrition, physical activity, and behaviour therapy (e.g., initiatives based on social cognitive theory) interventions, showed favourable outcomes for systolic and diastolic blood pressure, plasma glucose, and blood lipids (HDL-C, LDL-C, triglycerides, and total cholesterol) (202). <u>Lived experience</u>: Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (203-206). Reduction in mental health symptoms including depression and anxiety (207, 208), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (209-213). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (214-218). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (218-221). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (222-225). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (222, 223). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 202, 226, 227). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (226, 227).	Current available data indicates a reduction in eating disorder symptoms (binge eating) with weight management treatments. In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (228). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (228). Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (229), Healthy China Initiative (230), Finnish Diabetes Prevention Study (231)) overwhelmingly support positive health outcomes of physical activity. Additional benefits may include improved quality of life, and reduced depression and anxiety.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analyses:</u> No evidence was found in this population. <u>Additional undesirable effects:</u> Women with endometrial cancer participating in combined nutrition, physical activity, and behavioural interventions had a higher risk of musculoskeletal events (232). <u>Lived experience</u>:	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who

	Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (202, 216, 222). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (222, 223). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (227). Fears of embarrassment and failure during exercise activities were also reported (202, 220, 227, 233). Cultural and social expectations related to food and alcohol impacted adherence (216, 220, 234). Limited access to culturally appropriate and healthy foods (220), financial constraints (235), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (219, 226, 236-238).	are vulnerable to disordered eating and overexercising. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity and may set people back. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from meta-analysis:</u> The evidence is very uncertain about the effect of this intervention on adiposity. <u>Evidence from narrative synthesis:</u> Combined nutrition, physical activity, and psychological interventions may reduce adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving combined nutrition, physical activity, and psychological treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

o No important uncertainty or variability		
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favours the intervention o Varies o Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition, physical activity and psychological interventions are not necessarily widely available and affordable.	Long-term psychological care is often needed, and treatment is unlikely to be one-off. Costs are often borne by the patient and can be prohibitive. Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. Dietitians are expensive via the private system, and patients may experience a lack of access through the public health system. This treatment may be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours the intervention o Favours the intervention o Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased ● Varies o Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Equity is affected by cost and accessibility of treatments. Food security and cost of living affect equity. Healthy food remains inaccessible and/or unaffordable for disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. High cost of psychological care and long wait times may make treatment prohibitive for some people, decreasing health equity.

		Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition, physical activity, and psychological treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where nutrition, physical activity and psychological treatments are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition, physical activity and psychological interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to very low certainty of evidence:

Combined nutrition, physical activity and psychological interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8

19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1

41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045

66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097

90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316

115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150

139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107

164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Anderson AS, Craigie AM, Caswell S, Treweek S, Stead M, Macleod M, et al. The impact of a bodyweight and physical activity intervention (BeWEL) initiated through a national colorectal cancer screening programme: randomised controlled trial. BMJ. 2014;348(7950):g1823. doi: 10.1136/bmj.g1823
178. Bennett GG, Foley P, Levine E, Whiteley J, Askew S, Steinberg DM, et al. Behavioral treatment for weight gain prevention among black women in primary care practice: a randomized clinical trial. JAMA Intern Med. 2013;173(19):1770-7. doi: 10.1001/jamainternmed.2013.9263
179. Bennett GG, Warner ET, Glasgow RE, Askew S, Goldman J, Ritzwoller DP, et al. Obesity treatment for socioeconomically disadvantaged patients in primary care practice. Arch Intern Med. 2012;172(7):565-74. doi: 10.1001/archinternmed.2012.1
180. Christensen JR, Overgaard K, Carneiro IG, Holtermann A, Søgaard K. Weight loss among female health care workers- a 1-year workplace based randomized controlled trial in the FINALE-health study. BMC Public Health. 2012;12(1):625. doi: 10.1186/1471-2458-12-625
181. Dutton GR, Gowey MA, Tan F, Zhou D, Ard J, Perri MG, Lewis CE. Comparison of an alternative schedule of extended care contacts to a self-directed control: a randomized trial of weight loss maintenance. Int J Behav Nutr Phys Act. 2017;14:107. doi: 10.1186/s12966-017-0564-1
182. Fernández-Ruiz VE, Armero-Barranco D, Paniagua-Urbano JA, Sole-Agusti M, Ruiz-Sánchez A, Gómez-Marín J. Short-medium-long-term efficacy of interdisciplinary intervention against overweight and obesity: randomized controlled clinical trial. Int J Nurs Pract. 2018;24(6):e12690. doi: 10.1111/ijn.12690
183. Gilcharan Singh HK, Chee WSS, Hamdy O, Mechanick JI, Lee VKM, Barua A, et al. Eating self-efficacy changes in individuals with type 2 diabetes following a structured lifestyle intervention based on the transcultural Diabetes Nutrition Algorithm (tDNA): a secondary analysis of a randomized controlled trial. PLoS ONE. 2020;15(11):e0242487. doi: 10.1371/journal.pone.0242487
184. Howden EJ, Leano R, Petchey W, Coombes JS, Isbel NM, Marwick TH. Effects of exercise and lifestyle intervention on cardiovascular function in CKD. Clin J Am Soc Nephrol. 2013;8(9):1494-501. doi: 10.2215/CJN.10141012
185. Jiang X, Fan X, Wu R, Geng F, Hu C. The effect of care intervention for obese patients with type II diabetes. Medicine. 2017;96(42):e7524. doi: 10.1097/MD.0000000000007524

186. Kirby ML, Beatty S, Stack J, Harrison M, Greene I, McBrinn S, et al. Changes in macular pigment optical density and serum concentrations of lutein and zeaxanthin in response to weight loss. Br J Nutr. 2011;105(7):1036-46. doi: 10.1017/S0007114510004721
187. Mai K, Brachs M, Leupelt V, Jumpertz-von Schwartzenberg R, Maurer L, Grüters-Kieslich A, et al. Effects of a combined dietary, exercise and behavioral intervention and sympathetic system on body weight maintenance after intended weight loss: results of a randomized controlled trial. Metabolism. 2018;83:60-7. doi: 10.1016/j.metabol.2018.01.003
188. Moncrieft AE, Llabre MM, McCalla JR, Gutt M, Mendez AJ, Gellman MD, et al. Effects of a multicomponent life-style intervention on weight, glycemic control, depressive symptoms, and renal function in low-income, minority patients with type 2 diabetes: results of the Community Approach to Lifestyle Modification for Diabetes randomized controlled trial. Psychosom Med. 2016;78(7):851-60. doi: 10.1097/PSY.0000000000000348
189. Ockene IS, Tellez TL, Rosal MC, Reed GW, Mordes J, Merriam PA, et al. Outcomes of a Latino community-based intervention for the prevention of diabetes: the Lawrence Latino Diabetes Prevention Project. Am J Public Health. 2012;102(2):336-42. doi: 10.2105/AJPH.2011.300357
190. Reeves MM, Terranova CO, Winkler EAH, McCarthy N, Hickman IJ, Ware RS, et al. Effect of a remotely delivered weight loss intervention in early-stage breast cancer: randomized controlled trial. Nutrients. 2021;13(11):4091. doi: 10.3390/nu13114091
191. Ross R, Lam M, Blair SN, Church TS, Godwin M, Hotz SB, et al. Trial of prevention and reduction of obesity through active living in clinical settings: a randomized controlled trial. Arch Intern Med. 2012;172(5):414-24. doi: 10.1001/archinternmed.2011.1972
192. Santa-Maria CA, Coughlin JW, Sharma D, Armanios M, Blackford AL, Schreyer C, et al. The effects of a remote-based weight loss program on adipocytokines, metabolic markers, and telomere length in breast cancer survivors: the POWER-Remote trial. Clin Cancer Res. 2020;26(12):3024-34. doi: 10.1158/1078-0432.CCR-19-2935
193. Simpson SA, McNamara R, Shaw C, Kelson M, Moriarty Y, Randell E, et al. A feasibility randomised controlled trial of a motivational interviewing-based intervention for weight loss maintenance in adults. Health Technol Assess. 2015;19(50). doi: 10.3310/hta19500
194. Sniehotta FF, Evans EH, Sainsbury K, Adamson A, Batterham A, Becker F, et al. Behavioural intervention for weight loss maintenance versus standard weight advice in adults with obesity: a randomised controlled trial in the UK (NULevel Trial). PLoS Med. 2019;16(5):e1002793. doi: 10.1371/journal.pmed.1002793
195. Spring B, Pellegrini CA, Pfammatter A, Duncan JM, Pictor A, McFadden HG, et al. Effects of an abbreviated obesity intervention supported by mobile technology: the ENGAGED randomized clinical trial. Obesity. 2017;25(7):1191-8. doi: 10.1002/oby.21842
196. von Gruenigen V, Frasure H, Kavanagh MB, Janata J, Waggoner S, Rose P, et al. Survivors of uterine cancer empowered by exercise and healthy diet (SUCCEED): a randomized controlled trial. Gynecol Oncol. 2012;125(3):699-704. doi: 10.1016/j.ygyno.2012.03.042
197. Lombard C, Harrison C, Kozica S, Zoungas S, Ranasinha S, Teede H. Preventing Weight Gain in Women in Rural Communities: A Cluster Randomised Controlled Trial. PLoS Med. 2016;13(1):e1001941. doi: 10.1371/journal.pmed.1001941
198. Svetkey LP, Batch BC, Lin P-H, Intille SS, Corsino L, Tyson CC, et al. Cell phone intervention for you (CITY): a randomized, controlled trial of behavioral weight loss intervention for young adults using mobile technology. Obesity. 2015;23(11):2133-41. doi: 10.1002/oby.21226
199. Jiskoot G, Timman R, Beerthuizen A, Dietz de Loos A, Busschbach J, Laven J. Weight reduction through a cognitive behavioral therapy lifestyle intervention in PCOS: the primary outcome of a randomized controlled trial. Obesity. 2020;28(11):2134-41. doi: 10.1002/oby.22980
200. Hinderliter AL, Sherwood A, Craighead LW, Lin P-H, Watkins L, Babyak MA, Blumenthal JA. The long-term effects of lifestyle change on blood pressure: one-year follow-up of the ENCORE study. Am J Hypertens. 2014;27(5):734-41. doi: 10.1093/ajh/hpt183
201. Black MM, Hager ER, Wang Y, Hurley KM, Latta LW, Candelaria M, Caulfield LE. Toddler obesity prevention: a two-generation randomized attention-controlled trial. Matern Child Nutr. 2021;17(1):e13075. doi: 10.1111/mcn.13075
202. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
203. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
204. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
205. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261

206. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
207. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
208. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
209. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
210. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
211. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
212. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
213. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
214. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
215. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
216. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
217. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
218. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
219. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
220. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
221. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
222. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
223. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
224. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
225. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
226. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
227. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577

228. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
229. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
230. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
231. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
232. Agnew H, Kitson S, Crosbie EJ. Interventions for weight reduction in obesity to improve survival in women with endometrial cancer. Cochrane Database Syst Rev. 2023(3):CD012513. doi: 10.1002/14651858.CD012513.pub3
233. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
234. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
235. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
236. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
237. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
238. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition, physical activity and psychological compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interventions combining nutrition, physical activity and psychological	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Combined nutrition, physical activity and psychological interventions vs untreated comparator (baseline to 12 months) - meta-analysis												
21[a]	randomised trials	serious[b]	very serious[c]	not serious	not serious	none	4201	1904	-	Hedges' g 0.45 **lower** (0.68 lower to 0.23 lower)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.
Combined nutrition, physical activity and psychological interventions vs untreated comparator (baseline to 12 months) - narrative synthesis												
4[d]	randomised trials	serious[e]	serious[f]	not serious	not serious	none	4/4 studies found a positive effect for combining nutrition, physical activity and psychological interventions on weight maintenance/loss				⨁⨁◯◯ Low	Combined nutrition, physical activity and psychological interventions may reduce adiposity.

CI: confidence interval

Explanations

a. 21 studies, with 23 intervention arms
b. -1 using RoB-2 risk of bias rated Low (13 (25%) outcomes), Some concerns (26 (49%) outcomes), High (14 (26%) outcomes)
c. -2 Inconsistency of I^2= 92.25%
d. 4 studies, with 5 intervention arms
e. -1 using RoB-2 risk of bias rated Some concerns (3 (60%) outcomes), High (2 (40%) outcomes)
f. -1 due to unspecified heterogeneity due to differences in exposure

QUESTION

Should interventions combining nutrition, physical activity and family-centred vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and family-centred interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare.

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. Cardiovascular disease Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). Blood glucose level A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). Type 2 diabetes mellitus Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41).	

	Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45). <u>Non-alcoholic fatty liver disease</u> Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51). Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52). <u>Musculoskeletal conditions</u> Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56). <u>Cancer</u> When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)). Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had	

	poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis</u>: From 4 studies (177-180) with 315 intervention participants (adults) and 308 comparator participants, evidence demonstrated a trivial effect size of Hedges' g 0.18 lower (0.33 lower to 0.02 lower) in nutrition, physical activity, and family-centred interventions versus an untreated comparator. <u>Additional desirable effects</u>: No evidence was identified in this population. <u>Lived experience:</u>	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (207), Healthy China Initiative (208), Finnish Diabetes Prevention Study (209)) overwhelmingly support positive health outcomes of physical activity and

	Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (181-184). Reduction in mental health symptoms including depression and anxiety (185, 186), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (187-191). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (192-196). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (196-199). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (200-203). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (200, 201). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 204-206). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (205, 206).	In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (210). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (210). The benefits of weight loss or maintenance on cardiometabolic outcomes were also considered when making judgement.
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> No evidence was identified in this population. <u>Additional undesirable effects:</u> No evidence was identified in this population. <u>Lived experience:</u> Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (194, 200, 204). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (200, 201). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (206). Fears of embarrassment and failure during exercise activities were also reported (198, 204, 206, 211). Cultural and social expectations related to food and alcohol impacted adherence (194, 198, 212). Limited access to culturally appropriate and healthy foods (198), financial constraints (213), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (197, 205, 214-216).	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating and overexercising. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity with a goal to minimise risk of injury and stigma, while protecting mental health and engagement.

		Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Combined nutrition, physical activity, and family-centred interventions likely result in little to no difference in adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving combined nutrition, physical activity, and family-centred treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs	We have not sourced literature on the resources required for this intervention.	Dietitians are expensive via the private system, and

○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don’t know	Combined nutrition, physical activity and family-centred interventions are not necessarily widely available and affordable.	patients may experience a lack of access through the public health system. Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and/or unaffordable for

○ Increased ● Varies ○ Don't know		disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs; or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition, physical activity and family-centred treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where nutrition, physical activity and family-centred interventions are individually tailored and culturally appropriate. Accessibility of

		nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition, physical activity and family-centred interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Conditional recommendation for the intervention:

Combined nutrition, physical activity and family-centred interventions may be recommended as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8

19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1

41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005

67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21

91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434

116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017

141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034

166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Demark-Wahnefried W, Jones LW, Snyder DC, Sloane RJ, Kimmick GG, Hughes DC, et al. Daughters and Mothers Against Breast Cancer (DAMES): main outcomes of a randomized controlled trial of weight loss in overweight mothers with breast cancer and their overweight daughters. Cancer. 2014;120(16):2522-34. doi: 10.1002/cncr.28761
178. Rosas LG, Lv N, Xiao L, Lewis MA, Venditti EMJ, Zavella P, et al. Effect of a culturally adapted behavioral intervention for Latino adults on weight loss over 2 years: a randomized clinical trial. JAMA Netw Open. 2020;3(12):e2027744. doi: 10.1001/jamanetworkopen.2020.27744
179. Trief PM, Fisher L, Sandberg J, Cibula DA, Dimmock J, Hessler DM, et al. Health and psychosocial outcomes of a telephonic couples behavior change intervention in patients with poorly controlled type 2 diabetes: a randomized clinical trial. Diabetes Care. 2016;39(12):2165-73. doi: 10.2337/dc16-0035
180. Wake M, Lycett K, Clifford SA, Sabin MA, Gunn J, Gibbons K, et al. Shared care obesity management in 3-10 year old children: 12 month outcomes of HopSCOTCH randomised trial. BMJ. 2013;346:f3092. doi: 10.1136/bmj.f3092
181. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
182. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
183. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
184. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
185. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
186. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
187. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6

188. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
189. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
190. Palavras MA, Hay P, Filho CADS, Claudino A. The fficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
191. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
192. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
193. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
194. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
195. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
196. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
197. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
198. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
199. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
200. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
201. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
202. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
203. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
204. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
205. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
206. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
207. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
208. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
209. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
210. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473

211. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
212. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
213. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
214. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
215. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
216. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition, physical activity and family-centred compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	interventions **combining nutrition, physical activity and family-centred**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Combined nutrition, physical activity and family-centred interventions vs untreated comparator (baseline to 12 months)												
4[a]	randomised trials	serious[b]	not serious	not serious	not serious	none	315	308	-	Hedges' g **0.18 lower** (0.33 lower to 0.02 lower)	⨁⨁⨁◯ Moderate	Combined nutrition, physical activity and family-centred interventions likely results in little to no difference in adiposity.

CI: confidence interval

Explanations

a. 4 studies, 6 intervention arms
b. -1 using RoB-2 risk of bias rated Some concerns (9 (75%) outcomes), High (3 (25%) outcomes)

QUESTION

Should interventions combining nutrition, physical activity and sleep vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and sleep interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. Cardiovascular disease Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). Blood glucose level A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). Type 2 diabetes mellitus Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41).	

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45).

Non-alcoholic fatty liver disease

Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52).

Musculoskeletal conditions

Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56).

Cancer

When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had

	poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 3 studies (177-179) with 120 intervention participants and 127 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.46 lower (95%CI 1.45 lower to 0.53 higher) in nutrition, physical activity, and sleep interventions versus untreated comparator. <u>Additional evidence</u>: No evidence was identified in this population. <u>Lived experience:</u> No evidence from sleep interventions was identified in this population.	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (206), Healthy China Initiative (207), Finnish Diabetes Prevention Study (208)) overwhelmingly support positive health outcomes of physical activity and nutrition.

	Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (180-183). Reduction in mental health symptoms including depression and anxiety (184, 185), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (186-190). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (191-195). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (195-198). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (199-202). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (199, 200). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 203-205). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (204, 205).	The benefits of weight loss or maintenance on cardiometabolic outcomes were also considered when making judgement. In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg (209). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (209).
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analyses:</u> No evidence was identified in this population. <u>Additional undesirable effects:</u> No evidence was identified in this population. <u>Lived experience:</u> No evidence from sleep interventions was identified in this population. Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (193, 199, 203). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (199, 200). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (205). Fears of embarrassment and failure during exercise activities were also reported (197, 203, 205, 210). Cultural and social expectations related to food and alcohol impacted adherence (193, 197, 211). Limited access to culturally appropriate and healthy foods (197), financial constraints (212), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (196, 204, 213-215).	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change, increased physical activity, and improved sleep, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating and overexercising. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity with a goal to minimise risk of injury and stigma, while protecting mental health and

		engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. The evidence is very uncertain about the effect of combined nutrition, physical activity, and sleep interventions on adiposity.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving combined nutrition, physical activity, and sleep treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.
Resources required How large are the resource requirements (costs)?"		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on required resources. Combined nutrition, physical activity, and sleep interventions are not necessarily widely available and affordable.	Dietitians are expensive via the private system, and patients may experience a lack of access through the public health system. Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. Sleep studies and equipment are often inaccessible or unaffordable. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity: Healthy food remains inaccessible and/or unaffordable for disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. Sleep treatments and studies are often inaccessible or unaffordable, especially for disadvantaged or remote populations. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition, physical activity, and sleep treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where nutrition, physical activity and sleep treatment interventions are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition, physical activity and sleep interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to very low certainty of evidence:

Combined nutrition, physical activity and sleep interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8

19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1

41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045

66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097

90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316

115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150

139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107

164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Duncan MJ, Fenton S, Brown WJ, Collins CE, Glozier N, Kolt GS, et al. Efficacy of a multi-component m-health weight-loss intervention in overweight and obese adults: a randomised controlled trial. Int J Environ Res Public Health. 2020;17(17):6200. doi: 10.3390/ijerph17176200
178. Puhkala J, Kukkonen-Harjula K, Mansikkamäki K, Aittasalo M, Hublin C, Kärmeniemi P, et al. Lifestyle counseling to reduce body weight and cardiometabolic risk factors among truck and bus drivers--a randomized controlled trial. Scand J Work Environ Health. 2015;41(1):54-64. doi: 10.5271/sjweh.3463
179. Georgoulis M, Yiannakouris N, Kechribari I, Lamprou K, Perraki E, Vagiakis E, Kontogianni MD. Sustained improvements in the cardiometabolic profile of patients with obstructive sleep apnea after a weight-loss Mediterranean diet/lifestyle intervention: 12-month follow-up (6 months post-intervention) of the "MIMOSA" randomized clinical trial. Nutr Metab Cardiovasc Dis. 2023;33(5):1019-28. doi: 10.1016/j.numecd.2023.02.010
180. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
181. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
182. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
183. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
184. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150

185. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
186. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
187. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
188. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
189. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
190. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
191. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
192. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
193. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
194. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
195. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
196. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
197. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
198. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
199. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
200. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
201. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
202. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
203. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
204. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
205. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
206. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0

207. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
208. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
209. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
210. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
211. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
212. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
213. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
214. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
215. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition, physical activity and sleep compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interventions combining nutrition, physical activity and sleep	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Combined nutrition, physical activity and sleep interventions vs untreated comparator (baseline to 12 months)												
3[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	120	127	-	Hedges' g **0.46 lower** (1.45 lower to 0.53 higher)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 3 studies, with 3 intervention arms
b. -1 using RoB-2 risk of bias rated Low (2 (25%) outcomes), Some concerns (2 (25%) outcomes), High (4 (50%)
c. -1 Inconsistency of I^2= 64.82%
d. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)

QUESTION

Should a combination of four or more behavioural interventions vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	A combination of four or more behavioural interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. Cardiovascular disease Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). Blood glucose level A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). Type 2 diabetes mellitus Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41).	

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45).

Non-alcoholic fatty liver disease

Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52).

Musculoskeletal conditions

Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56).

Cancer

When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had

	poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis:</u> From 7 studies (177-183) with 807 intervention participants and 790 comparator participants, evidence demonstrated a small unimportant effect of Hedges' g 0.16 lower (0.3 lower to 0.02 lower) in the intervention versus untreated comparator. <u>Evidence from narrative synthesis:</u> 2 additional studies (184, 185) unable to be included in the meta-analysis found a positive effect of combining four or more behavioural interventions for weight maintenance/loss.	Less is known about the effects of multimodal approaches to weight management, due in part to study heterogeneity and low availability of evidence. However, some patients may be encouraged to take up multimodal treatments with specific tailoring to their needs.

	<u>Additional desirable effects</u>: No evidence was identified in this population. <u>Lived experience</u>: Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (186-189). Reduction in mental health symptoms including depression and anxiety (190, 191), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (192-196). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (197-201). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (201-204). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (205-208). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (205, 206). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 209-211). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (210, 211).	In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (212). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (212). Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (213), Healthy China Initiative (214), Finnish Diabetes Prevention Study (215)) overwhelmingly support positive health outcomes of physical activity and nutrition.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analyses:</u> No evidence was identified in this population. <u>Additional undesirable effects</u>: No evidence was identified in this population. <u>Lived experience</u>: Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (199, 205, 209). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (205, 206). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (211). Fears of embarrassment and failure during exercise activities were also reported (203, 209, 211, 216). Cultural and social expectations related to food and alcohol impacted adherence (199, 203, 217). Limited access to culturally appropriate and healthy foods (203), financial constraints (218), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (202, 210, 219-221).	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating and overexercising. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight

		or obesity with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from meta-analysis:</u> A combination of four or more behavioural interventions may result in little to no difference in adiposity. <u>Evidence from narrative synthesis</u>: The evidence is very uncertain about the effect of this intervention on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving a combination of four or more behavioural interventions. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise,

intervention o Varies o Don't know		particularly strengthening activities.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. A combination of four or more behavioural interventions are not necessarily widely available and affordable.	Dietitians are expensive via the private system, and patients may experience a lack of access through the public health system. Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. Long-term psychological care is often needed, and treatment is unlikely to be one-off. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison	No evidence on the cost effectiveness of this intervention was identified for this population.	

o Probably favours the intervention o Favours the intervention o Varies ● No included studies		

Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased ● Varies o Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Equity is affected by cost of treatments and accessibility of treatments. Food security and cost of living affect equity. Healthy food remains inaccessible and/or unaffordable for disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. High cost of psychological care and long wait times may make treatment prohibitive for some people, decreasing health equity. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs; or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment; etc Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or

		disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving a combination of four or more behavioural interventions. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where multiple interventions (including nutrition, physical activity, family-centred, psychological, and sedentary behaviour) are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of a combination of 4 or more behavioural interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Conditional recommendation for the intervention:

Combined multimodal (four or more) behavioural interventions may be recommended as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8

19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1

41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005

67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21

91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434

116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017

141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034

166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Duncan S, Goodyear-Smith F, McPhee J, Grøntved A, Schofield G. Family-centered brief intervention for reducing obesity and cardiovascular disease risk: a randomized controlled trial. Obesity. 2016;24(11):2311-8. doi: 10.1002/oby.21602
178. French SA, Sherwood NE, Veblen-Mortenson S, Crain AL, JaKa MM, Mitchell NR, et al. Multicomponent obesity prevention intervention in low-income preschoolers: primary and subgroup analyses of the NET-Works randomized clinical trial, 2012-2017. Am J Public Health. 2018;108(12):1695-706. doi: 10.2105/AJPH.2018.304696
179. Haire-Joshu D, Schwarz CD, Steger-May K, Lapka C, Schechtman K, Brownson RC, Tabak RG. A randomized trial of weight change in a national home visiting program. Am J Prev Med. 2018;54(3):341-51. doi: 10.1016/j.amepre.2017.12.012
180. Neale EP, Tapsell LC, Martin A, Batterham MJ, Wibisono C, Probst YC. Impact of providing walnut samples in a lifestyle intervention for weight loss: a secondary analysis of the HealthTrack trial. Food Nutr Res. 2017;61(1). doi: 10.1080/16546628.2017.1344522
181. Tapsell LC, Lonergan M, Batterham MJ, Neale EP, Martin A, Thorne R, et al. Effect of interdisciplinary care on weight loss: a randomised controlled trial. BMJ Open. 2017;7(7):e014533. doi: 10.1136/bmjopen-2016-014533
182. Verweij LM, Proper KI, Weel ANH, Hulshof CTJ, van Mechelen W. Long-term effects of an occupational health guideline on employees' body weight-related outcomes, cardiovascular disease risk factors, and quality of life: results from a randomized controlled trial. Scand J Work Environ Health. 2013;39(3):284-94. doi: 10.5271/sjweh.3341
183. Maddison R, Hargreaves EA, Jiang Y, Calder AJ, Wyke S, Gray CM, et al. Rugby Fans in Training New Zealand (RUFIT NZ): a randomized controlled trial to assess the effectiveness of a healthy lifestyle program for overweight men delivered through professional rugby clubs. Int J Behav Nutr Phys Act. 2023;20(1):37. doi: 10.1186/s12966-022-01395-w
184. Black MM, Hager ER, Wang Y, Hurley KM, Latta LW, Candelaria M, Caulfield LE. Toddler obesity prevention: a two-generation randomized attention-controlled trial. Matern Child Nutr. 2021;17(1):e13075. doi: 10.1111/mcn.13075
185. Hanvold SE, Vinknes KJ, Løken EB, Hjartåker A, Klungsøyr O, Birkeland E, et al. Does lifestyle intervention after gastric bypass surgery prevent weight regain? A randomized clinical trial. Obes Surg. 2019;29(11):3419-31. doi: 10.1007/s11695-019-04109-7
186. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
187. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
188. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261

189. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
190. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
191. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
192. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
193. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
194. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
195. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
196. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
197. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
198. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
199. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
200. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
201. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
202. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
203. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
204. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
205. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
206. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
207. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
208. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
209. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
210. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473

211. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
212. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
213. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
214. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
215. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
216. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
217. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
218. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
219. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
220. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
221. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: A combination of four or more behavioural interventions compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	multimodal interventions **combining four or more interventions**	treated/untreated **comparators**	Relative (95% CI)	**Absolute** (95% CI)		
Four or more **behavioural** interventions vs **untreated comparator (baseline to 12 months)** – Meta-analysis												
7[a]	randomised trials	serious[b]	serious[c]	not serious	not serious	none	807	790	-	Hedges' g **0.16 lower** (0.3 lower to 0.02 lower)	⊕⊕◯◯ Low	Combining four or more interventions may result in little to no difference in adiposity
Four or more **behavioural interventions vs untreated comparator (baseline to 12 months)** – Narrative synthesis												
2[d]	randomised trials	serious[e]	serious[f]	not serious	serious[g]	none	2/2 studies found a positive effect of combining four or more interventions for weight maintenance/loss				⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity

CI: confidence interval

Explanations

a. 7 studies, with 9 intervention arms
b. -1 using RoB-2 risk of bias rated Low (2 (11%) outcomes), Some concerns (9 (50%) outcomes), High (7 (39%) outcomes)
c. -1 Inconsistency of I^2=45.18%
d. 2 studies, with 2 intervention arms
e. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
f. -1 due to unspecified heterogeneity due to differences in exposure
g. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should interventions combining nutrition and family-centred vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Combined nutrition and family-centred interventions vs untreated comparators (baseline to final end-point)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). <u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41).	

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45).

Non-alcoholic fatty liver disease

Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52).

Musculoskeletal conditions

Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56).

Cancer

When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had

	poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from narrative synthesis:</u> 1 study (177) with 3 intervention arms unable to be included in a meta-analysis found mixed effects. 2 intervention arms favoured a combination of nutrition and family-centred interventions, 1 intervention arm had a negative effect compared to the comparator for weight maintenance/loss. <u>Additional desirable effects:</u> No evidence was identified in this population. <u>Lived experience:</u>	In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (204). Similarly, in adults taking part in weight loss physical activity

	Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (178-181). Reduction in mental health symptoms including depression and anxiety (182, 183), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (184-188). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (189-193). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (193-196). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (197-200). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (197, 198). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 201-203). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (202, 203).	interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (204). Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (205), Healthy China Initiative (206), Finnish Diabetes Prevention Study (207)) overwhelmingly support positive health outcomes of physical activity and nutrition.
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from narrative synthesis: 1 study (177) with 3 intervention arms unable to be included in a meta-analysis found mixed effects. 2 intervention arms favoured a combination of nutrition and family-centred interventions, 1 intervention arm had a negative effect compared to the comparator for weight maintenance/loss. Additional undesirable effects: No evidence was identified in this population. Lived experience: Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (191, 197, 201). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (197, 198). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (203). Fears of embarrassment and failure during exercise activities were also reported (195, 201, 203, 208). Cultural and social expectations related to food and alcohol impacted adherence (191, 195, 209). Limited access to culturally appropriate and healthy foods (195), financial constraints (210), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (194, 202, 211-213).	In addition to intentional adiposity loss, some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss. When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change and family-involvement, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from narrative synthesis:</u> Combined nutrition and family-centred interventions may result in little to no difference in adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving nutrition and family-centred treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition and family-centred interventions are not necessarily widely available and affordable.	Dietitians are expensive via the private system, and patients may experience a lack of access through the public health system. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited.

		Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness
Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living. Access to healthy food is still unaffordable for disadvantaged populations. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

		Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition and family-centred treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where nutrition is individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of nutrition and family-centred interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation
Consensus statement due to limited evidence: Combined nutrition and family-centred interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8

19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1

41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005

67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21

91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434

116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017

141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034

166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Jenkins DJA, Boucher BA, Ashbury FD, Sloan M, Brown P, El-Sohemy A, et al. Effect of current dietary recommendations on weight loss and cardiovascular risk factors. J Am Coll Cardiol. 2017;69(9):1103-12. doi: 10.1016/j.jacc.2016.10.089
178. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
179. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
180. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
181. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
182. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
183. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
184. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
185. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
186. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
187. Palavras MA, Hay P, Filho CADS, Claudino A. The fficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299

188. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
189. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
190. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
191. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
192. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
193. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
194. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
195. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
196. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
197. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
198. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
199. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
200. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
201. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
202. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
203. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
204. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
205. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
206. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
207. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
208. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
209. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
210. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
211. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347

212. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
213. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition and family-centred compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Combined nutrition and family-centred interventions vs untreated comparators (baseline to final end-point)									
1[a]	randomised trials	very serious[b]	not serious	not serious	not serious	none	1 study with 3 intervention arms showed mixed effects.2 intervention arms favoured a combination of nutrition and family-centred interventions, 1 intervention arm had a negative effect compared to the comparator for weight maintenance/loss.	⨁⨁◯◯ Low	Combined nutrition and family-centred interventions may result in little to no difference in adiposity.

CI: confidence interval

Explanations

a. 1 study, with 3 intervention arms
b. -2 using RoB-2 risk of bias rated High (1 (100%) outcom

QUESTION

Should interventions combining nutrition and psychological interventions vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Combined nutrition and psychological interventions vs untreated comparator (baseline to final end-point)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare.

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). <u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41).	

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45).

Non-alcoholic fatty liver disease

Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52).

Musculoskeletal conditions

Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56).

Cancer

When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had

	poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from narrative synthesis:</u> 1 study (177) unable to be included in a meta-analysis favoured combining nutrition and psychological interventions. Weight reduced by 1.1 kgs in the intervention arm and 0.9 kgs in the comparator arm. <u>Additional desirable effects:</u> No evidence was identified in this population. <u>Lived Experience:</u> Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical	Current available data indicates a reduction in eating disorder symptoms (binge eating) with weight management treatments. The benefits of weight loss or maintenance on cardiometabolic outcomes were also considered when

	function, and reduced body pain (178-181). Reduction in mental health symptoms including depression and anxiety (182, 183), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (184-188). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (189-193). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (193-196). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (197-200). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (197, 198). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 201-203). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (202, 203).	making judgement. In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (204).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis:</u> No evidence was identified in this population. <u>Additional undesirable effects</u>: No evidence was identified in this population. <u>Lived Experience:</u> Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (191, 197, 201). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (197, 198). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (203). Fears of embarrassment and failure during exercise activities were also reported (195, 201, 203, 205). Cultural and social expectations related to food and alcohol impacted adherence (191, 195, 206). Limited access to culturally appropriate and healthy foods (195), financial constraints (207), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (194, 202, 208-210).	In addition to intentional adiposity loss, some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss. When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change and psychological treatment, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table.	

○ High ○ No included studies	The evidence is very uncertain about the effect of combined nutrition and psychological interventions on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not systematically collected scientific evidence regarding patients' preferences and values in relation to receiving combined nutrition and psychological treatment. However, the committee believes that since there are benefits most patients would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition and psychological interventions are not necessarily widely available and affordable.	Dietitians are expensive via the private system, and patients may experience a lack of access through the public health system. Long term psychological care is often required, and treatment is unlikely to be one-off. This treatment is likely to be cost effective but due to current resource constraints within the public health

		system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours the intervention o Favours the intervention o Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased ● Varies o Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity: Healthy food remains inaccessible and/or unaffordable for disadvantaged or remote populations. High cost of psychological care and long wait times may make treatment prohibitive for some people, decreasing health equity. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups,

		along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available programs; or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition and psychological treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where nutrition and psychological treatment is individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition and psychological interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation
<u>Consensus statement due to limited evidence:</u> Combined nutrition and psychological interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8

19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1

41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005

67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21

91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434

116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017

141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034

166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Bräutigam-Ewe M, Lydell M, Bergh H, Hildingh C, Baigi A, Månsson J. Two-year weight, risk and health factor outcomes of a weight-reduction intervention programme: primary prevention for overweight in a multicentre primary healthcare setting. Scand J Prim Health Care. 2020;38(2):192-200. doi: 10.1080/02813432.2020.1753379
178. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
179. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
180. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
181. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
182. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
183. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
184. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
185. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
186. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201

187. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
188. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
189. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
190. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
191. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
192. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
193. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
194. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
195. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
196. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
197. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
198. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
199. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
200. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
201. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
202. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
203. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
204. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
205. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
206. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
207. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
208. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
209. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
210. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition and psychological interventions compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Combined nutrition and psychological interventions vs untreated comparator (baseline to final end-point)									
1[a]	randomised trials	very serious[b]	not serious	not serious	serious[c]	none	1/1 study favoured combining nutrition and psychological interventions. Weight reduced by 1.1 kgs in the intervention arm and 0.9 kgs in the comparator arm.	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity

CI: confidence interval

Explanations

a. 1 study, with 1 intervention arm
b. -2 using RoB-2 risk of bias rated High for all studies
c. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should interventions combining physical activity and psychological interventions vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity ?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Combined physical activity and psychological interventions vs untreated comparators (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle aged adults. <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). <u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41).	

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45).

<u>Non-alcoholic fatty liver disease</u>
Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52).

<u>Musculoskeletal conditions</u>
Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56).

<u>Cancer</u>
When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41) cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had

	poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). Mental health Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). Health-related quality of life ratings Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). Reproductive health Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from narrative synthesis: 1 of 2 additional studies (177, 178) unable to be included in a meta-analysis favoured combining physical activity and psychological interventions for weight maintenance/loss, 1 of 2 additional studies unable to be included in a meta-analysis found a negative effect compared to the comparator arm. Additional desirable effects; No evidence was identified in this population.	In young and middle-aged adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (205).

	Lived experience: Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (179-182). Reduction in mental health symptoms including depression and anxiety (183, 184), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (185-189). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (190-194). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (194-197). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (198-201). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (198, 199). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (167, 202-204). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (203, 204).	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (206), Healthy China Initiative (207), Finnish Diabetes Prevention Study (208)) overwhelmingly support positive health outcomes of physical activity. Current available data indicates a reduction in eating disorder symptoms (binge eating) with weight management treatments.
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from meta-analyses: No evidence was identified in this population. Additional undesirable effects: No evidence was identified in this population. Lived experience: Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (192, 198, 202). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (198, 199). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (204). Fears of embarrassment and failure during exercise activities were also reported (196, 202, 204, 209). Cultural and social expectations related to food and alcohol impacted adherence (192, 196, 210). Limited access to culturally appropriate and healthy foods (196), financial constraints (211), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (195, 203, 212-214).	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates increased physical activity, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to overexercising. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity with a goal to minimise risk of injury and stigma, while protecting mental health and engagement.

		Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. The evidence is very uncertain about the effect of combined physical activity and psychological interventions on adiposity.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving combined physical activity, and psychological treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.
Resources required How large are the resource requirements (costs)?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know	We have not sourced literature on the resources required for this intervention. Combined physical activity and psychological interventions are not necessarily widely available and affordable.	Participant-reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. Long-term psychological care is often needed and treatment is unlikely to be one-off. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	High costs of gym memberships, club fees and

○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know		equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. High cost of psychological care and long wait times may make treatment prohibitive for some people, decreasing health equity. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined physical activity and psychological treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where physical activity is individually tailored and appropriate. Acceptable where mental health is considered.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined physical activity and psychological interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	**Probably favours the comparison**	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	**Varies**	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation
<u>Consensus statement due to limited evidence:</u> Combined physical activity and psychological interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8

19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1

41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005

67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21

91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434

116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017

141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034

166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Arredondo EM, Haughton J, Ayala GX, Slymen D, Sallis JF, Perez LG, et al. Two-year outcomes of Faith in Action/Fe en Acción: a randomized controlled trial of physical activity promotion in Latinas. Int J Behav Nutr Phys Act. 2022;19:97. doi: 10.1186/s12966-022-01329-6
178. López Tarraga PJ, Madrona-Marcos F, Panisello-Royo J, Carbayo-Herencia JA, Rosich N, Tarraga-Marcos L, et al. [Evaluation of a motivational intervention of physical activity program in the treatment of obesity and overweight]. Hipertens Riesgo Vasc. 2020;37(1):11-6. doi: 10.1016/j.hipert.2019.05.003
179. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
180. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
181. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
182. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
183. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
184. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
185. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
186. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020

187. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
188. Palavras MA, Hay P, Filho CADS, Claudino A. The fficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
189. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
190. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
191. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
192. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
193. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
194. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
195. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
196. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
197. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
198. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
199. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
200. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
201. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
202. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
203. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
204. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
205. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
206. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
207. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
208. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
209. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114

210. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
211. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
212. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
213. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
214. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining physical activity and psychological interventions compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Combined physical activity and psychological interventions vs untreated comparators (baseline to 12 months)									
2[a]	randomised trials	very serious[b]	serious[c]	not serious	not serious	none	1/2 studies favoured combining physical activity and psychological interventions for weight maintenance/loss, 1 study found a negative effect compared to the comparator arm.	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 2 studies, with 2 intervention arms
b. -2 using RoB-2 risk of bias rated Some concerns (1 (50%) study, High (1 (50%) study)
c. -1 due to unspecified heterogeneity due to differences in exposur

QUESTION

Should pharmacological interventions vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Pharmacological interventions: **Pharmacological interventions approved for the treatment of overweight or obesity:** • Liraglutide, 3.0mg per day (subcutaneous) intervention vs any comparator (baseline to 12 months) • Orlistat, 360mg per day interventions vs any comparator (baseline to 12 months) • Naltrexone, 32mg plus Bupropion, 360mg per day interventions vs any comparator (baseline to 12 months) • Anorectic and Anticonvulsant drug class interventions vs any comparator (baseline to final end-point) • Phentermine, 7.5mg plus Topiramate, 46.0mg per day intervention vs any comparator (baseline to final end-point) • Phentermine, 15.0mg plus Topiramate, 92.0mg per day intervention vs any comparator (baseline to final end-point) • Semaglutide, 2.4mg per week (subcutaneous) intervention vs any comparator (baseline to final end-point) • Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonists drug class interventions vs any comparator (baseline to final end-point) • Tirzepatide, 5mg per week intervention (subcutaneous) vs any comparator (baseline to final end-point) • Tirzepatide, 10mg per week (subcutaneous) intervention vs any comparator (baseline to final end-point) • Tirzepatide, 15mg per week (subcutaneous) intervention vs any comparator (baseline to final end-point)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Guideline Development Committee members with potential Conflicts of Interest as detailed in 'Management of competing interests' section of the Guideline document participated in discussions but were not part of final recommendation development.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19).	

	Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). <u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41). Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45). <u>Non-alcoholic fatty liver disease</u> Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51). Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52). <u>Musculoskeletal conditions</u> Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56). <u>Cancer</u> When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)). Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41)	

	cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a	

	healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Pharmacological interventions approved for the treatment of overweight or obesity: ○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	**Pharmacological interventions approved for the treatment of overweight or obesity (by drug class and drug type, where applicable):** ***Evidence from baseline to 12 months:*** **<u>Liraglutide</u>** <u>Evidence from meta-analyses:</u> From 3 studies (177-179) with 301 intervention participants and 235 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.67 lower (95% CI 0.83 lower to 0.5 lower) in Liraglutide 3.0mg per day (subcutaneous) versus any comparator. **<u>Naltrexone plus Bupropion</u>** <u>Evidence from meta-analyses:</u> From 1 study (180) with 684 intervention participants and 633 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.61 lower (95% CI 0.72 lower to 0.5 lower) in Naltrexone, 32mg plus Bupropion, 360mg per day versus any comparator. **<u>Orlistat</u>** <u>Evidence from narrative synthesis:</u> 1 additional study (181) unable to be included in the meta-analysis found a positive effect of Orlistat 360mg per day on weight maintenance/loss. ***Evidence from baseline to final end-point:*** **<u>Anorectic and anticonvulsant drug class</u>** <u>Evidence from meta-analyses:</u> From 1 study (182) with 1469 intervention participants and 979 comparator participants, evidence demonstrated a large effect size of Hedges' g 0.9 lower (95% CI 1.05 lower to 0.74 lower) in anorectic and anticonvulsant drug class interventions versus any comparator. **<u>Phentermine plus topiramate:</u>** <u>Evidence from narrative synthesis:</u> 1 additional study (182) unable to be included in the meta-analysis found a positive effect of phentermine, 7.5mg plus topiramate, 46.0mg per day on weight maintenance/loss. <u>Evidence from narrative synthesis:</u> 1 additional study (182) unable to be included in the meta-analysis found a positive effect of phentermine, 15.0mg plus topiramate, 92.0mg per day on weight maintenance/loss. **<u>Semaglutide:</u>** <u>Evidence from meta-analyses:</u>	Clinicians should be aware that each drug class has a different profile of additional benefits which may be relevant when prescribing. Weight loss is typically lower in people living with Type 2 diabetes mellitus compared to those without diabetes, however health benefits are still experienced. Some drugs used for treatment of Type 2 diabetes mellitus (e.g. semaglutide, liraglutide) are prescribed in lower dosages than for the treatment of obesity, however patients may have weight loss benefits at these dosages. Studies of other medications approved for weight management (phentermine) and those commonly used off-label (e.g. topiramate) did not qualify for inclusion in this review. Additional studies demonstrated cardiovascular benefits, including reduction in CV mortality, however these studies did not meet inclusion criteria of this review.

	From 4 studies (183-186) with 870 intervention participants and 726 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.79 lower (95% CI 1.47 lower to 0.1 lower) in semaglutide 2.4 mg per week (subcutaneous) versus any comparator. <u>Evidence from narrative synthesis:</u> 2 additional studies (187, 188) unable to be included in the meta-analysis found a positive effect of semaglutide, 2.4mg per week (subcutaneous) on weight maintenance/loss. <u>**Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonists drug class:**</u> <u>Evidence from meta-analyses:</u> From 3 studies (189-191) with 2806 intervention participants and 1250 comparator participants, evidence demonstrated a large effect size of Hedges' g 1.23 lower (95% CI 1.52 lower to 0.93 lower) in glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonists interventions versus any comparator. <u>**Tirzepatide:**</u> <u>Evidence from narrative synthesis:</u> 1 additional study (190) unable to be included in the meta-analysis found a positive effect of Tirzepatide 5mg per week (subcutaneous) on weight maintenance/loss. <u>Evidence from meta-analyses:</u> From 2 studies (189, 190) with 948 intervention participants and 958 comparator participants, evidence demonstrated a large effect size of Hedges' g 1.02 lower (95% CI 1.17 lower to 0.87 lower) in Tirzepatide 10mg per week (subcutaneous) versus any comparator. <u>Evidence from meta-analyses:</u> From 3 studies (189-191) with 1228 intervention participants and 1250 comparator participants, evidence demonstrated a large effect size of Hedges' g 1.44 lower (95% CI 2.43 lower to 0.44 lower) in Tirzepatide 15mg per week (subcutaneous) versus any comparator. *Additional evidence:* Specific medications had reported beneficial outcomes for type 2 diabetes (lipase inhibitors (192), anorectic and anticonvulsants (192), GLP-1 [semaglutide] (192), and biguanide (43, 193), cardiovascular mortality (opioid antagonist plus norepinephrine-dopamine reuptake inhibitor (192)), global HRQoL (opioid antagonist plus norepinephrine-dopamine reuptake inhibitor (192)) and physical function (GLP-1 [semaglutide] (194)), systolic blood pressure (anorectic and anticonvulsants (192), GLP-1 [semaglutide and liraglutide] (192), and biguanide (193)), diastolic blood pressure (lipase inhibitors (192), anorectic and anticonvulsants (192), and GLP-1 [semaglutide and liraglutide] (192)), fasting glucose (lipase inhibitors (195) and biguanide (193)), HDL-C (lipase inhibitors (192), anorectic and anticonvulsants (192), GLP-1 [semaglutide and liraglutide] (192), and opioid antagonist plus norepinephrine-dopamine reuptake inhibitor (192)), LDL-C (lipase inhibitors (192)), and total cholesterol (lipase inhibitors (192)). For young and middle-aged adults with type 2 diabetes participating in pharmacological weight management/loss interventions, specific medications had favourable outcomes for systolic and diastolic blood pressure (GLP-1 receptor agonists [semaglutide] (196)), fasting plasma glucose levels (lipase inhibitors (197)), and HbA1c (lipase inhibitors (192) and GLP-1 receptor agonists [semaglutide and liraglutide] (192)).	

	Reported favourable outcomes for young and middle-aged adults without type 2 diabetes participating in pharmacological weight management/loss interventions involving GLP-1 receptor agonists (liraglutide, semaglutide) were reduced systolic and diastolic blood pressure, reduced fasting blood glucose, increased HDL-C, and reduced LDL-C and triglycerides (198). <u>Lived experience:</u> Studies of adults engaged in pharmacological interventions showed increases in health-related quality of life, physical functioning, and mental functioning (199-201).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Pharmacological interventions approved for the treatment of overweight or obesity: ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Adverse outcomes reported in reviews of pharmacological interventions were increased systolic and diastolic blood pressure with opioid antagonist plus norepinephrine-dopamine reuptake inhibitor (192), and adverse events with various medications (192-195). Specifically in adults without type 2 diabetes, adverse outcomes with GLP-1 receptor agonists (liraglutide, semaglutide) were increased nausea, vomiting, diarrhoea, constipation, abdominal pain, dyspepsia, hypoglycaemia, and neoplasms (198). <u>Lived experience:</u> No evidence was identified in this population	Clinicians should be aware each drug class has a different profile of adverse effects, which may be relevant when prescribing. Medication-related adverse effects are common, most are mild and often transient. Many adverse effects can be minimised or mitigated by starting at a low dose followed by a gradual increase. In addition to intentional adiposity loss, some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss. Regular review of medication and long-term follow-up are necessary. Awareness of possible drug-drug interactions is necessary. These differ by drug class. There is very limited long-term data from pharmacological studies. Evidence is rapidly evolving - need for regular revision.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Pharmacological interventions	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table.	

approved for the treatment of overweight or obesity: ○ Very low ○ Low ● Moderate ● High ○ No included studies	**Pharmacological interventions approved for the treatment of overweight or obesity:** Evidence from meta-analysis: ***Anorectic and Anticonvulsant drug class*** The following interventions likely results in a large reduction in adiposity: • Anorectic and Anticonvulsants ***Opioid antagonist plus Norepinephrine-dopamine reuptake inhibitor drug class*** The following interventions likely reduces adiposity: • Opioid antagonist plus Norepinephrine-dopamine reuptake inhibitors (Naltrexone, 32mg plus Bupropion, 360mg per day) ***Glucagon-like peptide-1 (GLP-1) receptor agonists drug class*** The following interventions likely reduces adiposity: • Liraglutide, 3.0mg per day (subcutaneous) The following interventions results may reduce adiposity: • Semaglutide, 2.4mg per week (subcutaneous) ***Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonists drug class*** The following interventions likely results in a large reduction in adiposity: • Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonists • Tirzepatide, 10mg per week (subcutaneous) The following interventions likely results in a large reduction in adiposity: • Tirzepatide, 15mg per week (subcutaneous) Evidence from narrative synthesis: ***Anorectic and Anticonvulsant drug class*** The following interventions likely reduces adiposity: • Phentermine, 7.5mg plus Topiramate, 46.0mg per day. • Phentermine, 15.0mg plus Topiramate, 92.0mg per day. ***Lipase inhibitors drug class interventions*** The following interventions may result in a large reduction in adiposity • Orlistat 360mg per day ***Glucagon-like peptide-1 (GLP-1) receptor agonists drug class*** The following interventions likely reduces adiposity: • Semaglutide, 2.4mg per week (subcutaneous) ***Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonists drug class*** The following interventions likely results in a reduction in adiposity: • Tirzepatide, 5mg per week (subcutaneous)	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on patients' preferences and values in relation to receiving pharmacological interventions. However, the committee believes that since there are benefits this treatment should be considered for all patients where clinically appropriate.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management. A lack of availability for people who meet treatment guidelines has highlighted the widespread demand/unmet need for pharmacological interventions.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Pharmacological interventions approved for the treatment of overweight or obesity: ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the Committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resource requirements for pharmacological interventions for overweight or obesity.	Currently there is no subsidisation of pharmacological interventions by the PBS, and the entire treatment cost is covered by patients. Off-label use of Topiramate alone is common because of cost and availability of alternative weight management medications. This treatment is likely to be cost effective (although can

		vary) but due to current resource constraints within the public health system, treatment access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ● Varies ○ No included studies	Cost effectiveness data is presented by study rather than by medication because studies differ in what inputs they used (e.g., medication effectiveness data, estimates of associations between BMI and quality of life), and their time horizons. Note that quality adjusted life years (QALYs) are calculated using estimates of the change in QALYs per BMI unit lost (i.e., this figure is constant throughout calculations in a given study) and change in BMI with various pharmaceutical interventions. Therefore, QALYs are a proxy for the effectiveness of pharmaceutical interventions. In a cost-effectiveness analysis from a US provider perspective (202), the QALYs gained over a lifetime horizon (unspecified length of time) were 17.83 years for semaglutide (2.4mg weekly, subcutaneous), 17.34 years for liraglutide (3.0mg daily, subcutaneous), 17.38 years for phentermine (7.5/15mg daily) plus topiramate (46mg/92mg daily), and 17.16 years for bupropion (32mg daily) plus naltrexone (360mg daily). In comparison, the QALYs gained with behavioural modification were 16.93 years. In a cost-effectiveness analysis from a US payer's perspective (203), the QALYs gained over a lifetime horizon (40 years) from five anti-obesity medications (tirzepatide, semaglutide, liraglutide, phentermine plus topiramate, and naltrexone plus bupropion) differed less than 0.5 years. The QALYs ranged from 29.6 years for tirzepatide (subcutaneous) to 29.2 years for naltrexone plus bupropion. Medication doses were not provided. In a cost-effectiveness analysis in a US setting (204), the QALYs gained (presumably over a week) were 0.0083 years for semaglutide (1.0mg weekly, subcutaneous), 0.0032 years for liraglutide (1.8mg daily, subcutaneous), and 0.0053 years for dulaglutide (1.5mg weekly, subcutaneous). The change in QALYs with no treatment was -0.0002. In a cost-effectiveness analysis from a US third party payer perspective (205), the QALYs gained over a 30-year time horizon were 13.49 for semaglutide (2.4mg, subcutaneous), 13.35 years for liraglutide (3mg, subcutaneous), 13.35 years for phentermine plus topiramate, and 13.34	

	years for naltrexone plus bupropion. The change in QALYs with diet and exercise was 13.31 years and with no treatment was 12.57 years. In a cost-effectiveness analysis from a US healthcare system cost perspective (206), the QALYs gained over a 5-year time horizon were 3.71 years for semaglutide (0.4mg daily, subcutaneous), 3.63 years for liraglutide (3.0mg daily, subcutaneous), 3.63 years for orlistat (120mg three times daily), and 3.66 years for phentermine plus topiramate (7.5mg/46mg daily). The change in QALYs with intensive behavioural intervention was 3.66 years and with no treatment was 3.59 years. In a cost-effectiveness analysis from a Canadian societal perspective (207), the QALYs gained over a 40-year time horizon were 18.32 years for semaglutide (2.4mg, subcutaneous), 18.27 years for liraglutide (3.0 mg, subcutaneous), 18.23 years for naltrexone plus bupropion (32mg/360mg), and 18.22 years for orlistat. The change in QALYs with diet and exercise was 18.18 years. No approved obesity medications are listed on the PBS.	
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Widely available and accessible pharmacological interventions increase health equity. However, large barriers to accessibility of pharmacological interventions exist for many people. The need to self-fund treatment decreases equity. Current drug costs and reimbursement structures of medications are a barrier to equity. When discussing the patient's care plan, practitioners should take into consideration whether the patient may face out-of-pocket expenses (i.e. gap payments) when accessing the prescribed treatment, etc. Equity could also be addressed by raising the patient's awareness of available adjunct treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups,

		along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving pharmacological interventions. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians, where clinically appropriate.	Stigma may reduce acceptability of this treatment to patients and clinicians. Some patients or clinicians may not deem pharmacological interventions for weight management in adults to be acceptable. Acceptability increases where interventions (including adjunct interventions) are individually tailored and culturally appropriate. For example, increased accessibility of affordable pharmacological treatment increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of pharmacological interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Medication shortages and supply issues may decrease feasibility of pharmacological interventions. Current pharmacological intervention costs and reimbursement structures of medications are a barrier to feasibility.

		Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	**High**			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	**Varies**	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

CONCLUSIONS

Recommendation

Strong recommendation for the intervention:

Pharmacological interventions, approved by the TGA for weight management, should be considered as part of a comprehensive treatment program to improve weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8

19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1

41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005

67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21

91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434

116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017

141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034

166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Lundgren JR, Janus C, Jensen SBK, Juhl CR, Olsen LM, Christensen RM, et al. Healthy weight loss maintenance with exercise, liraglutide, or both combined. N Engl J Med. 2021;384(18):1719-30. doi: 10.1056/NEJMoa2028198
178. O'Neil PM, Birkenfeld AL, McGowan B, Mosenzon O, Pedersen SD, Wharton S, et al. Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: a randomised, double-blind, placebo and active controlled, dose-ranging, phase 2 trial. Lancet. 2018;392(10148):637-49. doi: 10.1016/S0140-6736(18)31773-2
179. Wadden TA, Walsh OA, Berkowitz RI, Chao AM, Alamuddin N, Gruber K, et al. Intensive behavioral therapy for obesity combined with liraglutide 3.0 mg: a randomized controlled trial. Obesity. 2019;27(1):75-86. doi: 10.1002/oby.22359
180. Wharton S, Batterham RL, Bhatta M, Buscemi S, Christensen LN, Frias JP, et al. Two-year effect of semaglutide 2.4 mg on control of eating in adults with overweight/obesity: STEP 5. Obesity. 2023;31(3):703-15.
181. Derosa G, Cicero AF, D'Angelo A, Fogari E, Maffioli P. Effects of 1-year orlistat treatment compared to placebo on insulin resistance parameters in patients with type 2 diabetes. J Clin Pharm Ther. 2012;37(2):187-95. doi: 10.1111/j.1365-2710.2011.01280.x
182. Gadde KM, Allison DB, Ryan DH, Peterson CA, Troupin B, Schwiers ML, Day WW. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. Lancet. 2011;377(9774):1341-52. doi: 10.1016/S0140-6736(11)60205-5
183. Davies M, Færch L, Jeppesen OK, Pakseresht A, Pedersen SD, Perreault L, et al. Semaglutide 2·4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. Lancet. 2021;397(10278):971-84. doi: 10.1016/S0140-6736(21)00213-0
184. Rubino DM, Greenway FL, Khalid U, O'Neil PM, Rosenstock J, Sørrig R, et al. Effect of weekly subcutaneous semaglutide vs daily liraglutide on body weight in adults with overweight or obesity without diabetes: the STEP 8 randomized clinical trial. JAMA. 2022;327(2):138-50. doi: 10.1001/jama.2021.23619
185. Garvey WT, Batterham RL, Bhatta M, Buscemi S, Christensen LN, Frias JP, et al. Two-year effects of semaglutide in adults with overweight or obesity: the STEP 5 trial. Nat Med. 2022;28(10):2083-91. doi: 10.1038/s41591-022-02026-4
186. Wilding JPH, Batterham RL, Davies M, Van Gaal LF, Kandler K, Konakli K, et al. Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. Diabetes Obes Metab. 2022;24(8):1553-64.
187. Wadden TA, Bailey TS, Billings LK, Davies M, Frias JP, Koroleva A, et al. Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: the STEP 3 randomized clinical trial. JAMA. 2021;325(14):1403-13. doi: 10.1001/jama.2021.1831
188. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med. 2021;384(11):989-1002. doi: 10.1056/NEJMoa2032183

189. Garvey WT, Frias JP, Jastreboff AM, le Roux CW, Sattar N, Aizenberg D, et al. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet. 2023;402(10402):613-26. doi: 10.1016/S0140-6736(23)01200-X
190. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. Tirzepatide once weekly for the treatment of obesity. N Engl J Med. 2022;387(3):205-16. doi: 10.1056/NEJMoa2206038
191. Wadden TA, Chao AM, Machineni S, Kushner R, Ard J, Srivastava G, et al. Tirzepatide after intensive lifestyle intervention in adults with overweight or obesity: the SURMOUNT-3 phase 3 trial. Nat Med. 2023;29(11):2909-18. doi: 10.1038/s41591-023-02597-w
192. Iannone A, Natale P, Palmer SC, Nicolucci A, Rendina M, Giorgino F, et al. Clinical outcomes associated with drugs for obesity and overweight: a systematic review and network meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2023;25(9):2535-44. doi: 10.1111/dom.15138
193. Leblanc ES, O'Connor E, Whitlock EP, Patnode CD, Kapka T. Effectiveness of primary care-relevant treatments for obesity in adults: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2011;155(7):434-47. doi: 10.7326/0003-4819-155-7-201110040-00006
194. He K, Guo Q, Zhang H, Xi W, Li J, Jing Z. Once-weekly semaglutide for obesity or overweight: a systematic review and meta-analysis. Diabetes Obes Metab. 2022;24(4):722-6. doi: 10.1111/dom.14612
195. Zhou Y-H, Ma X-Q, Wu C, Lu J, Zhang S-S, Guo J, et al. Effect of anti-obesity drug on cardiovascular risk factors: a systematic review and meta-analysis of randomized controlled trials. PLoS ONE. 2012;7(6):e39062. doi: 10.1371/journal.pone.0039062
196. Tsapas A, Karagiannis T, Kakotrichi P, Avgerinos I, Mantsiou C, Tousinas G, et al. Comparative efficacy of glucose-lowering medications on body weight and blood pressure in patients with type 2 diabetes: a systematic review and network meta-analysis. Diabetes Obes Metab. 2021;23(9):2116-24. doi: 10.1111/dom.14451
197. Aldekhail NM, Logue J, McLoone P, Morrison DS. Effect of orlistat on glycaemic control in overweight and obese patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. Obes Rev. 2015;16(12):1071-80. doi: 10.1111/obr.12318
198. Iqbal J, Wu H-X, Hu N, Zhou Y-H, Li L, Xiao F, et al. Effect of glucagon-like peptide-1 receptor agonists on body weight in adults with obesity without diabetes mellitus-a systematic review and meta-analysis of randomized control trials. Obes Rev. 2022;23(6):e13435. doi: 10.1111/obr.13435
199. Fabricatore AN, Wadden TA, Higginbotham AJ, Faulconbridge LF, Nguyen AM, Heymsfield SB, Faith MS. Intentional weight loss and changes in symptoms of depression: a systematic review and meta-analysis. Int J Obes. 2011;35(11):1363-76. doi: 10.1038/ijo.2011.2
200. Warkentin LM, Das D, Majumdar SR, Johnson JA, Padwal RS. The effect of weight loss on health-related quality of life: systematic review and meta-analysis of randomized trials. Obes Rev. 2014;15(3):169-82. doi: 10.1111/obr.12113
201. Zhong P, Zeng H, Huang M, Fu W, Chen Z. Efficacy and safety of once-weekly semaglutide in adults with overweight or obesity: a meta-analysis. Endocrine. 2022;75(3):718-24. doi: 10.1007/s12020-021-02945-1
202. Atlas SJ, Kim K, Nhan E, Touchette DR, Moradi A, Agboola F, et al. Medications for obesity management: Effectiveness and value. J Manag Care Spec Pharm. 2023;29(5):569-75. doi: 10.18553/jmcp.2023.29.5.569
203. Gómez Lumbreras A, Tan MS, Villa-Zapata L, Ilham S, Earl JC, Malone DC. Cost-effectiveness analysis of five anti-obesity medications from a US payer's perspective. Nutr Metab Cardiovasc Dis. 2023;33(6):1268-76. doi: 10.1016/j.numecd.2023.03.012
204. Hu Y, Zheng S-L, Ye X-L, Shi J-N, Zheng X-W, Pan H-S, et al. Cost-effectiveness analysis of 4 GLP-1RAs in the treatment of obesity in a US setting. Ann Transl Med. 2022;10(3):152.
205. Kim N, Wang J, Burudpakdee C, Song Y, Ramasamy A, Xie Y, et al. Cost-effectiveness analysis of semaglutide 2.4 mg for the treatment of adult patients with overweight and obesity in the United States. J Manag Care Spec Pharm. 2022;28(7):740-52. doi: 10.18553/jmcp.2022.28.7.740
206. Lee M, Lauren BN, Zhan T, Choi J, Klebanoff M, Abu Dayyeh B, et al. The cost-effectiveness of pharmacotherapy and lifestyle intervention in the treatment of obesity. Obes Sci Pract. 2020;6(2):162-70. doi: 10.1002/osp4.390
207. Olivieri A-V, Muratov S, Larsen S, Luckevich M, Chan K, Lamotte M, Lau DCW. Cost-effectiveness of weight-management pharmacotherapies in Canada: a societal perspective. Int J Obes. 2024;48(5):683-93. doi: 10.1038/s41366-024-01467-w

Question: Pharmacological interventions compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pharmacological interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Liraglutide, 3.0mg (sc) per day intervention vs any comparator (baseline to 12 months) - meta-analysis												
3[a]	randomised trials	serious[b]	not serious	not serious	not serious	none	301	235	-	Hedges' g **0.67 lower** (0.83 lower to 0.5 lower)	⊕⊕⊕◯ Moderate	Liraglutide, 3.0mg per day (subcutaneous) likely reduces adiposity
Lipase inhibitors drug class (Orlistat, 360mg per day) interventions vs any comparator (baseline to 12 months) - narrative synthesis												
1[c]	randomised trials	serious[d]	not serious	not serious	serious[e]	none	1/1 study found a positive effect of lipase inhibitors on weight maintenance/loss Weight reduced by 9.5kgs in the intervention arm compared to a weight gain of 2.6kgs in the comparator arm				⊕⊕◯◯ Low	Lipase inhibitors drug class interventions may result in a large reduction in adiposity
Opioid antagonist plus Norepinephrine-dopamine reuptake inhibitor drug class (Naltrexone, 32mg plus Bupropion, 360mg per day) interventions vs any comparator (baseline to 12 months) - meta-analysis												
1[f]	randomised trials	very serious[g]	not serious	not serious	not serious	strong association	684	633	-	Hedges' g **0.61 lower** (0.72 lower to 0.5 lower)	⊕⊕⊕◯ Moderate	Opioid antagonist plus Norepinephrine-dopamine reuptake inhibitor drug class interventions likely reduces adiposity
Anorectic and Anticonvulsant drug class interventions vs any comparator (baseline to final end-point) - meta-analysis												
1[f]	randomised trials	very serious[g]	not serious	not serious	not serious	strong association	1469	979	-	Hedges' g **0.9 lower** (1.05 lower to 0.74 lower)	⊕⊕⊕◯ Moderate	Anorectic and Anticonvulsant drug class interventions likely results in a large reduction in adiposity.
Phentermine, 7.5mg plus Topiramate, 46.0mg per day intervention vs any comparator (baseline to final end-point) - narrative synthesis												
1[c]	randomised trials	very serious[g]	not serious	not serious	not serious	strong association	1/1 study found a positive effect of Phentermine, 7.5mg plus Topiramate, 46.0mg per day on weight maintenance/loss. The intervention arm decreased in body weight by 7.8% compared to 1.2% in the placebo/comparator arm.				⊕⊕⊕◯ Moderate	Phentermine, 7.5mg plus Topiramate, 46.0mg per day likely reduces adiposity
Phentermine, 15.0mg plus Topiramate, 92.0mg per day intervention vs any comparator (baseline to final end-point) - narrative synthesis												
1[c]	randomised trials	very serious[g]	not serious	not serious	not serious	strong association	1/1 study found a positive effect of Phentermine, 15mg plus Topiramate, 92.0mg per day on weight maintenance/loss. The intervention arm decreased in body by 9.8% compared to 1.2% in the placebo/comparator arm.				⊕⊕⊕◯ Moderate	Phentermine, 15mg plus Topiramate, 92.0mg per day likely reduces adiposity .
Semaglutide, 2.4mg per week (sc) intervention vs any comparator (baseline to final end-point) - meta-analysis												
4[h]	randomised trials	not serious	very serious[i]	not serious	not serious	none	870	726	-	Hedges' g **0.79 lower** (1.47 lower to 0.1 lower)	⊕⊕◯◯ Low	Semaglutide, 2.4mg per week (subcutaneous) may reduce adiposity
Semaglutide, 2.4mg per week (sc) intervention vs any comparator (baseline to final end-point)- narrative synthesis												
2[j]	randomised trials	not serious	serious[k]	not serious	not serious	none	2/2 studies found a positive effect of semaglutide, 2.4mg per week on weight maintenance/loss				⊕⊕⊕◯ Moderate	Semaglutide, 2.4mg per week (subcutaneous) likely reduces adiposity.
Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonists drug class interventions vs any comparator (baseline to final end-point)-meta-analysis												
3[l]	randomised trials	serious[m]	very serious[n]	not serious	not serious	very strong association	2806	1250	-	Hedges' g **1.23 lower** (1.52 lower to 0.93 lower)	⊕⊕⊕◯ Moderate	Glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonists drug class interventions likely result in a large reduction in adiposity.
Tirzepatide, 5mg per week (sc) intervention vs any comparator (baseline to final end-point)-narrative synthesis												

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	pharmacological interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
1[c]	randomised trials	serious[d]	not serious	not serious	not serious	strong association	1/1 study found positive effects for tirzepatide, 5mg per week (subcutaneous) on weight maintenance/loss. The intervention arm decreased body weight by 15.0% compared to 3.1% in the placebo/comparator arm.				⨁⨁⨁⨁ High	Tirzepatide, 5mg per week (subcutaneous) results in a reduction in adiposity
Tirzepatide, 10mg per week (sc) intervention vs any comparator (baseline to final end-point) -meta-analysis												
2[j]	randomised trials	not serious	serious[o]	not serious	not serious	very strong association	948	958	-	Hedges' g **1.02 lower** (1.17 lower to 0.87 lower)	⨁⨁⨁⨁ High	Tirzepatide, 10mg per week (subcutaneous) results in a large reduction in adiposity.
Tirzepatide, 15mg per week (sc) intervention vs any comparator (baseline to final end-point) -meta-analysis												
3[p]	randomised trials	serious[q]	very serious[r]	not serious	not serious	very strong association	1228	1250	-	Hedges' g **1.44 lower** (2.43 lower to 0.44 lower)	⨁⨁⨁◯ Moderate	Tirzepatide, 15mg per week (subcutaneous) likely results in a large reduction in adiposity.

CI: confidence interval

Explanations

a. 3 studies, with 5 intervention arms
b. -1 using RoB-2 risk of bias rated Low (8 (42%) outcomes), Some concerns (11 (58%) outcomes)
c. 1 study, with 1 intervention arm
d. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
e. -1 Imprecision due to small sample size (Total n<400)
f. 1 study, with 2 intervention arms
g. -2 using RoB-2 risk of bias all outcomes rated High
h. 4 studies, with 4 intervention arms
i. -2 Inconsistency of I^2=99.19%
j. 2 studies, with 2 intervention arms
k. -1 for unspecified heterogeneity due to differences in exposure
l. 3 studies, with 6 intervention arms
m. -1 using RoB-2 risk of bias rated Low (8 (47%) outcomes), Some concerns (9 (53%) outcomes)
n. -2 Inconsistency of I^2=94.45%
o. -1 Inconsistency of I^2=62.52%
p. 3 studies, with 3 intervention arms
q. -1 using RoB-2 risk of bias rated Low (4 (44%) outcomes), Some concerns (5 (56%) outcomes)
r. -2 Inconsistency of I^2=96.33%
s. 1 study, with 1 intervention

QUESTION

Should surgical interventions vs. treated/untreated comparators be used for weight maintenance/loss in young and middle-aged adults experiencing overweight or obesity?	
POPULATION:	Young and middle-aged adults living with overweight or obesity
INTERVENTION:	Surgical interventions: • **Bariatric surgery intervention vs medical treatment (baseline to 12 months)** • Laparoscopic adjustable gastric banding (LAGB) versus best medical treatment (baseline to 12 months) • Roux-en-Y Gastric Bypass (RYGB) surgery versus best medical treatment (baseline to 12 months) • Sleeve Gastrectomy (SG) versus best medical treatment (baseline to 12 months) • Stapled laparoscopic mini-gastric bypass-one anastomosis gastric bypass (LMGB-OAGB) versus best medical treatment (baseline to 12 months) • **Bariatric surgery plus adjunct therapy intervention vs bariatric surgery plus usual care/placebo (baseline to 12 months)** • Biliopancreatic diversion with duodenal switch (BPD-DS) or sleeve gastrectomy (SG) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 months) • Laparoscopic Roux-en-Y gastric bypass (LRYGB) or sleeve gastrectomy (SG) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 months) • Roux-en-Y Gastric Bypass (RYGB) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 months) • Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 months) • **Endoscopic surgery intervention versus medical treatment (baseline to 12 months)** • Duodenal-jejunal bypass liner (EndoBarrier) versus best medical treatment (baseline to 12 months) • g-CathEZ delivery catheter with snowshoe suture anchors versus best medical treatment (baseline to 12 months) • Endoscopic sleeve gastroplasty versus best medical treatment (baseline to 12 months) • Percutaneous gastrostomy device versus best medical treatment (baseline to 12 months) • Intragastric balloon therapy versus best medical treatment (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Guideline Development Committee members with potential Conflicts of Interest as detailed in 'Management of competing interests' section of the Guideline document participated in discussions but were not part of final recommendation development.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in young and middle-aged adults. <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (1-12). Cardiovascular disease mortality increased with increasing weight (11, 13-15). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (16, 17), including ischemic stroke (16), and haemorrhagic stroke (16). Risk was also elevated for coronary artery disease (18, 19).	

	Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (20). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (21). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (5, 22-24). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (25). <u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (9, 19, 26-41). Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (5, 25, 42-45). <u>Non-alcoholic fatty liver disease</u> Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (46-51). Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (52-54). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (52). <u>Musculoskeletal conditions</u> Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (55). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (56). <u>Cancer</u> When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (57, 58), thyroid (58-64), and blood cancers such as; lympho-haematopoietic (65) and diffuse large B-cell lymphoma (66, 67), multiple myeloma (58, 67-69), Hodgkin and non-Hodgkin lymphoma (58, 67), and leukemia (70, 71) (obesity only (72)). Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (41, 57, 58, 63, 69, 70, 73-78), gastroesophageal (79, 80), gastric (58, 63, 78, 81, 82), and stomach (41)	

	cancers; and liver (41, 58, 63, 69, 80, 83-92), gallbladder (41, 58, 69, 70, 93-95), bile duct (96), pancreatic (41, 63, 69, 70, 80, 97-99), small intestinal (97), and colorectal (57, 58, 63, 69, 70, 80, 98, 100-117) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (41, 57, 58, 63, 69, 70, 80, 110, 118-122), and bladder (41, 58, 120, 121, 123-126)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (70) cancers, and total cancer risk was associated with increasing adiposity (127). Increased BMI in adulthood (≥18y) was protective against lung cancer (57, 128, 129), and pre-menopausal breast cancer (57, 130). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (131). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (132). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (58, 80, 133-136) (premenopausal (63, 137, 138) or postmenopausal (110) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (139). Risk of other gynaecological cancers also increased, including endometrial (57, 58, 69, 70, 107, 110, 140-143), uterine (41), and cervical cancers (58) (weak association with obesity (144)), as well as breast cancer (63, 70, 80, 107, 110, 127, 144-156). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (20). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (120, 157, 158), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (57, 159), while risk increased for development of advanced prostate cancer (80, 121, 159, 160) and prostate cancer mortality (161). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (162). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (163, 164), or depression (165, 166), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (162). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (167). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (168). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a	

	healthy body weight (169). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (170-174). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (175). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (176).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Bariatric surgery vs medical treatment ○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know **Endoscopic surgery interventions versus medical treatment:** ○ Trivial ○ Small ○ Moderate ○ Large ● Varies ○ Don't know **Bariatric surgery plus adjunct therapy versus bariatric surgery plus usual care/placebo** ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	**Bariatric surgery versus medical treatment:** <u>Evidence from meta-analysis</u>: From 16 studies (177-192) with 734 intervention participants and 567 comparator participants, evidence demonstrated a large effect size of Hedges' g 1.92 lower (2.32 lower to 1.52 lower) in bariatric surgery interventions versus medical treatment. From 5 studies (178, 180, 181, 190, 191) with 125 intervention participants and 132 comparator participants, evidence demonstrated a large effect size of Hedges' g 1.33 lower (2.3 lower to 0.36 lower) in laparoscopic adjustable gastric banding (LAGB) surgery interventions versus best medical treatment. From 11 studies (177-179, 182-186, 188, 189, 192) with 442 intervention participants and 435 comparator participants, evidence demonstrated a large effect size of Hedges' g 2.20 lower (2.63 lower to 1.76 lower) in Roux-en-Y gastric bypass (RYBG) surgery interventions versus best medical treatment. From 3 studies (186, 188, 192) with 147 intervention participants and 138 comparator participants, evidence demonstrated a large effect size of Hedges' g 2.18 lower (4.82 lower to 0.46 higher) in sleeve gastrectomy (SG) surgery interventions versus best medical treatment. <u>Evidence from narrative synthesis:</u> 1 additional study (187) unable to be included in a meta-analysis found a positive effect of stapled laparoscopic mini-gastric bypass-one anastomosis gastric bypass (LMGB-OAGB) on weight maintenance/loss. BMI decreased by 16.04 kg/m^2 in the intervention group versus 2.76 kg/m^2 in the comparator group. **Endoscopic surgery interventions versus medical treatment:** <u>Evidence from meta-analysis:</u> From 8 studies (193-200) with 578 intervention participants and 416 comparator participants, evidence demonstrated a large effect size of Hedges' g 0.88 lower (1.27 lower to 0.49 lower) in endoscopic surgery interventions versus best medical treatment. From 3 studies (194, 195, 197) with 126 intervention participants and 112 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.55 lower (1.19 lower to 0.09 higher) in duodenal-jejunal bypass liner (EndoBarrier) interventions versus best medical treatment. From 2 studies with 251 intervention participants and 120 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.55 lower (0.77 lower to 0.33 lower) in stapled g-CathEZ delivery	These positive research findings are also supported by evidence from multiple, large community-based longitudinal studies. (e.g., Swedish Obese Subjects Study, LABS). Some endoscopic devices appear to be more effective for weight loss than others. Differences between devices may lead to variability in results. Endoscopic therapies are in early-stage research.

catheter with snowshoe suture anchors interventions versus best medical treatment.

Evidence from narrative synthesis:
1 additional study (200) unable to be included in a meta-analysis found a positive effect of endoscopic sleeve gastroplasty on weight maintenance/loss. Mean weight loss was 13.4kg in intervention arm versus 0.8kg in the comparator arm

1 additional study (200) unable to be included in a meta-analysis found a positive effect of a percutaneous gastrostomy device on weight maintenance/loss. Mean weight loss was 14.2kg in the intervention arm versus 4.1kg in the comparator arm.

1 additional study (201) unable to be included in a meta-analysis found a positive effect of intragastric balloon therapy on weight maintenance/loss. Total body weight loss (%) was 10.6% in the intervention arm versus 3.3% in the comparator arm.

Bariatric surgery plus adjunct therapy versus bariatric surgery plus usual care/placebo:
Evidence from meta-analysis:
From 2 studies (202, 203) with 63 intervention participants and 115 comparator participants, evidence demonstrated a small unimportant effect of Hedges' g 0.16 lower (0.98 lower to 0.66 higher) in laparoscopic Roux-en-Y gastric bypass (LRYGB) or sleeve gastrectomy (SG) plus adjunct therapy versus bariatric surgery plus usual care/placebo.

Evidence from narrative synthesis:
1 additional study (204) unable to be included in a meta-analysis found a positive effect of biliopancreatic diversion with duodenal switch (BPD-DS) or sleeve gastrectomy (SG) plus adjunct therapy intervention on weight loss/maintenance. Mean weight change at 12 months was 42.3kg in the intervention arm versus 38.4kg in the comparator arm.

1 additional study (205) unable to be included in a meta-analysis found a small positive effect of Roux-en-Y Gastric Bypass (RYGB) plus adjunct therapy compared to bariatric surgery plus usual care/placebo on weight maintenance/loss. BMI decreased by 16.62kg/m^2 in the intervention arm, versus 16.36kg/m^2 in the comparator group

Additional desirable effects:
Bariatric surgery has produced favourable outcomes for cardiovascular disease (e.g., coronary artery disease (206), atrial fibrillation (207), myocardial infarction (206), and stroke (208)), type 2 diabetes (e.g., type 2 diabetes risk (209) and diabetes remission (210)), adverse liver outcomes risk (211), non-alcoholic cirrhotic disease risk (211), knee pain (212), overall cancer risk and risk of various cancer types (e.g., colorectal, pancreatic, gallbladder and ovarian cancers) (213), cardiovascular (206) and cancer-related (213) mortality, HRQoL (e.g., global HRQoL (210), physical functioning (214), social functioning (214), and emotional functioning (214)), blood pressure indicators (e.g., systolic and diastolic blood pressure (215) and hypertension remission (216)), glucose metabolism (fasting glucose (217, 218) and HbA1c (210, 218)), dyslipidaemia incidence (209), and reduction in use of lipid lowering medications (210).

	For young and middle-aged adults with type 2 diabetes participating in bariatric surgery, there were favourable outcomes for cardiovascular disease (atrial fibrillation (207), coronary heart disease (219), and macrovascular complications risk (220)), type 2 diabetes (e.g., diabetes remission (219, 221)), all-cause mortality (220), systolic blood pressure (222), HbA1c (222), and blood lipids (dyslipidaemia remission (222), HDL-C (222), and triglycerides (222)). In Chinese adults with type 2 diabetes, Roux-en-Y gastric bypass was shown to increase diabetes remission, and reduce in systolic and diastolic blood pressure, HbA1c, fasting plasma glucose, and triglycerides (223). Women participating in surgical interventions had increased recovery from work-restricting knee pain with bariatric surgery (212). <u>Lived experience:</u> Studies of individuals who have had bariatric surgery interventions have shown improvements in overall health-related quality of life, including reduced depression (224-230) and anxiety (231, 232), and a decrease in eating disorder behaviours such as binge eating and emotional eating (233, 234). Improvements in body image, self-esteem, and psychosocial experiences, such as romantic relationships have also been reported (235-239). Participants reported a sense of relief upon achieving weight loss goals and noted benefits from improved physical abilities, capacity to achieve activities of daily living, fitting into seats and average-sized clothing, increased fertility, and reduction in co-morbidities such as Type 2 diabetes mellitus, and associated medication use (235-240). Pre- and postoperative counselling was associated with improved wellbeing and functioning post-surgery (241, 242). Supportive networks were considered important for successful weight loss and psychological wellbeing (235, 236, 239, 243, 244).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Bariatric surgery vs usual care /placebo: ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know **Endoscopic surgery interventions versus medical treatment:** ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know **Bariatric surgery plus adjunct therapy versus bariatric**	<u>Evidence from meta-analysis:</u> Bariatric surgery plus adjunct therapy versus bariatric surgery plus usual care/placebo: From 9 studies (202-204, 245-250) with 472 intervention participants and 502 comparator participants, evidence demonstrated a small unimportant effect of Hedges' g 0.04 higher (0.1 lower to 0.19 higher) in bariatric surgery plus adjunct therapy versus bariatric surgery plus usual care/placebo. From 3 studies (245, 247, 249) with 172 intervention participants and 168 comparator participants, evidence demonstrated a small unimportant effect of Hedges' g 0.14 higher (0.79 lower to 1.08 higher) in Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) plus adjunct therapy versus bariatric surgery plus usual care/placebo. <u>Evidence from narrative synthesis</u>: 1 additional study (246) unable to be included in a meta-analysis found a negative effect of Laparoscopic Roux-en-Y gastric bypass (LRYGB) plus adjunct therapy compared to bariatric surgery plus usual care/placebo on weight maintenance/loss. BMI decreased by 13.5 kg/m^2 in the intervention arm versus 14.5 kg/m^2 in the comparator arm.	In addition to intentional adiposity loss, some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss Evidence from large, observational, longitudinal studies (257, 259) have determined that there is an excess of mortality from suicide from some surgery types . Broader substance misuse has been documented in observational studies.

surgery plus usual care/placebo ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	1 additional study (251) unable to be included in a meta-analysis found Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) plus adjunct therapy compared to bariatric surgery plus usual care/placebo on weight maintenance/loss Intervention arm lost 30.9% of their body weight versus 31.2% in the comparator arm <u>Additional undesirable effects:</u> Undesirable effects associated with bariatric surgery were increased cirrhosis risk (211) and breast cancer (stage I) risk (252), as well as surgery-related adverse events (253, 254). There were increased serious adverse events with bariatric surgery in people with type 2 diabetes (222). Undesirable effects for Chinese adults with type 2 diabetes participating in bariatric surgery were increased surgical complication rates and mortality (223). <u>Lived experience:</u> Studies of participants who had bariatric surgery interventions reported higher rates of unpleasant gastrointestinal symptoms (235, 238, 242, 244), issues related to excess skin (255, 256), and higher rates of suicide and self-harm post-surgery. Conditions such as dumping syndrome, vomiting, reflux, and pain after eating were also noted (235, 238, 242, 244). Additionally, some participants reported increased risks of vitamin and mineral deficiencies, and osteoporosis (237, 238, 256). Participants reported negative effects of having excess skin such as increased body dissatisfaction, body dysmorphia, psychological distress, infection, discomfort, and restricted mobility (235-237). Individuals with pre-existing mental health issues were more likely to experience exacerbation or persistence of these concerns after surgery (244, 257, 258). Some participants reported overuse or abuse of alcohol as a coping mechanism in place of food (236, 242, 244). Relationship challenges were identified, leading to social avoidance and self-isolation (235, 236).	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Bariatric surgery versus best medical treatment interventions ○ Very low ● Low ○ Moderate ○ High ○ No included studies **Endoscopic surgery versus best medical treatment interventions** ● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. ***<u>Bariatric surgery versus best medical treatment interventions:</u>*** • Bariatric surgery versus best medical treatment interventions may result in a large reduction in adiposity with a low certainty of evidence. The following interventions may result in a large reduction in adiposity: • Laparoscopic adjustable gastric banding (LAGB). • Roux-en-Y gastric banding (RYGB). • Sleeve gastrectomy (SG). The following intervention results in a large reduction in adiposity: • Stapled laparoscopic mini-gastric bypass-one anastomosis gastric bypass (LMGB-OAGB). ***<u>Endoscopic surgery versus best medical treatment interventions</u>***: • The evidence is very uncertain about the effect of endoscopic surgery on adiposity. The following intervention results in a large reduction in adiposity:	

Bariatric surgery plus adjunct therapy versus bariatric surgery plus usual care/ placebo interventions ○ Very low ● Low ○ Moderate ○ High ○ No included studies	• Percutaneous gastrostomy device. The following interventions likely results in a large reduction in adiposity: • Endoscopic sleeve gastroplasty. • Intragastric balloon therapy. The following interventions may reduce adiposity: • g-CathEZ delivery catheter with snowshoe suture anchors. The evidence is very uncertain about the effect of the following interventions on adiposity: • Duodenal-jejunal bypass liner (EndoBarrier) intervention on adiposity. ***<u>Bariatric surgery plus adjunct therapy versus bariatric surgery plus usual care/ placebo interventions:</u>*** Bariatric surgery plus adjunct therapy interventions may result in little to no difference in adiposity versus bariatric plus usual care/placebo. The following interventions likely results in a large reduction in adiposity: • Laparoscopic Roux-en-Y gastric bypass (LRYGB) plus adjunct therapy. • Roux-en-Y gastric bypass (RYGB) plus adjunct therapy. The evidence is very uncertain about the effect of the following interventions on adiposity: • Biliopancreatic diversion with duodenal switch (BPD-DS) or sleeve gastrectomy (SG) plus adjunct therapy. • Laparoscopic Roux-en-Y gastric bypass (LRYGB) or sleeve gastrectomy (SG) plus adjunct therapy. • Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) plus adjunct therapy.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with obesity in relation to receiving bariatric surgery. However, the committee believes that since there are benefits, some people living with moderate to severe obesity would opt for this treatment, where clinically appropriate.	The lived experience perspective supports this judgement. Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Bariatric surgery versus best medical treatment interventions	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the committee has reached a	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight

○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know	consensus decision that the balance between the desirable and undesirable effects favours the intervention.	loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities. Surgery plus adjunct versus surgery plus placebo/usual care: Our evidence has not considered other benefits/outcomes (e.g. body composition, mental health etc). A range of outcomes may be expected from different endoscopic surgery types.
Bariatric surgery plus adjunct therapy versus bariatric surgery plus usual care/ placebo interventions ○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the committee has reached a consensus decision that the balance between the desirable and undesirable effects does not favour either the intervention or the comparison.	
Endoscopic surgery versus best medical treatment interventions ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

● Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	We have not sourced literature on the resource requirements for bariatric surgery.	This treatment is likely to be cost effective but due to current resource constraints within the public health system, access to services may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it. Dietitians are expensive via the private system, and patients may experience a lack of access through the public health system. The committee's view is there are large upfront costs, however there are large savings.

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Bariatric surgery: ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ No included studies **Bariatric surgery plus adjunct therapy:** ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies **Endoscopic surgery:**	Affordability: Numerous studies internationally have evaluated the cost-effectiveness of bariatric surgery when compared to usual/non-surgical care (260-271). Such cost effectiveness analyses have focussed on bariatric surgery generally (260-264, 267, 269, 272) and/or examined cost effectiveness of specific types of bariatric surgery (268, 271, 273-277). One study conducted in Australia investigated cost effectiveness of adjustable gastric banding (AGB), Roux en Y gastric bypass (RYGB) and Sleeve Gastrectomy (SG) compared to usual care in people with obesity (268). Another study conducted in Australia investigated cost effectiveness of AGB compared to conventional therapy for management of type 2 diabetes (T2D) and obesity in people with comorbid T2D and obesity (278). Endoscopic therapy Compared to bariatric surgery, there is considerably less cost-effectiveness data on endoscopic therapies for obesity management. However, some recent studies have investigated the cost effectiveness of specific types of endoscopic therapies, including intra-gastric balloon (279), endoscopic sleeve gastrectomy (280), and duodenal–jejunal bypass liner (281). No studies on cost effectiveness of endoscopic therapies conducted in Australia were identified. *Methods of assessing cost effectiveness* Studies often assessed cost-effectiveness on the basis of incremental cost effectiveness ratios (ICERs). ICERs reflect the ratio of incremental cost between the intervention and comparator group (i.e. bariatric surgery and usual care, respectively) and the incremental effectiveness between the same groups. Incremental effectiveness is usually measured in terms of quality adjusted life years (QALYs) gained or disability-adjusted life years (DALYs) averted (282). When a treatment is determined to be both clinically superior and cost saving compared to comparator group, it may be regarded as an economically dominant strategy. Willingness-to-pay thresholds e.g. <$50,000 or <$100,000 USD are often employed in	

○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ● Varies ○ No included studies	analyses to represent what a payer is willing to pay. A recent systematic review (283) of cost effectiveness studies of bariatric surgery summarized cost effectiveness using a measure of incremental net monetary benefit (INB). INB reflects the net monetary benefit of the bariatric procedure compared to the comparator treatment (i.e. usual care), and can be calculated as the difference between incremental monetary benefit and incremental cost (283). Published cost effectiveness analyses varied with respect to the time horizon (e.g. <10 years, ≥10 years, or lifetime) and statistical models used (e.g. Markov model, or decision tree). Most studies used a base-case analysis, involved a payer perspective, (e.g. Healthcare system, or other third party payer) and discounted at a rate of 3-5% annually. *Study findings* • Bariatric surgery Numerous published studies report cost effectiveness of bariatric surgery in obesity management, as determined by bariatric surgery assuming dominance compared to usual care or with ICERs <$50,000 (USD equivalent), regardless of the time horizon (260-264, 267, 269-271, 277, 284). With a lifetime horizon, dominance and/or ICERs <$25,000 (USD equivalent) are frequently reported (260-264, 267, 269, 271, 272). Within these studies over a lifetime horizon, QALYs gained with bariatric surgery ranged from 0.5-5; and 0.5-1.1 life years gained were estimated. A recent systematic review reported a pooled incremental monetary benefit over a lifetime horizon of $101,897.96 (95% CI $79,390.93, $124,404.99; International dollars) for bariatric surgery generally when compared to usual care (283). When considered over a 10-year horizon, bariatric surgery was found to have a pooled incremental monetary benefit of $53,063.69 (95%CI 42,647.96, $63,479.43) when compared to usual care. In a recent systematic review focussing on T2D management in patients with comorbid obesity, it was reported that across studies with time horizons ranging from 2y to lifetime, ICERs for metabolic surgery were <€45,000 (Euro). However, most reported ICERs were <€20,000, with better outcomes over longer time horizons (285). • Roux-en-Y Gastric Bypass (RYGB) [includes LRYGB and ORYGB] Numerous studies have found RYGB surgeries to be cost-effective therapies compared to usual care/non-surgical treatment for individuals with obesity (265, 266, 268, 270, 273-277, 286, 287). ICERs showing dominance or <$50,000 (USD equivalent) with RYGB compared to usual care/non-surgical treatments over variable horizons were reported (265, 268, 270, 273, 274, 286, 287). A study in Australia reported an ICER of $22,645 for RYGB over a lifetime horizon (268). Within these aforementioned studies over a lifetime horizon, QALYs gained with RYGB surgeries ranged from 0.7-5.6. In a sub-group analysis within a recent systematic review, RYGB was found to have a non-statistically significant INB of $110,928.33 (95% CI −$8,677.49, $230,534.14) compared to usual care over a lifetime horizon (283). Some studies have demonstrated greater cost effectiveness of RYGB over other types of bariatric surgery (266, 273, 276, 286). • Laparoscopic adjustable gastric banding (LAGB) Numerous studies have found LAGB surgeries to be cost-effective therapies compared to usual care/non-surgical treatment for individuals with obesity (268, 270, 273, 276, 278, 287). ICERs showing dominance or <$50,000 (USD equivalent) with LAGB compared to usual care/non-surgical treatments over variable horizons were reported (268, 270, 273, 287). A study in Australia reported an ICER of $24,454 for AGB over a lifetime horizon (268). In another Australian study, the calculated mean discounted lifetime costs of AGB were $98,900 AUD per surgical therapy patient with comorbid obesity and type 2 diabetes and $101,400 AUD per	

conventional therapy patient with comorbid obesity and type 2 diabetes (278). A mean health care saving of $2,400 AUD and 1.2 additional QALYs per patient was established with surgical weight loss treatment compared to conventional therapy. In a sub-group analysis within a recent systematic review, AGB was found to have a statistically significant INB of $51,143.29 (95% CI$15,735.29, $86,551.29 International dollars) compared to usual care over a lifetime horizon (283).

- Sleeve Gastrectomy (SG)

Some studies have found SG to be cost-effective therapies compared to usual care/non-surgical treatment for individuals with obesity (268, 270, 273, 288). A study in Australia reported an ICER of $27,523 AUD for SG over a lifetime horizon (268). In a sub-group analysis within a recent systematic review, SG was found to have a statistically significant INB of $127,578.98 (95% CI$62,139.61, $193,018.36 International dollars) compared to usual care over a lifetime horizon (283). Using an activity-based funding model, a study conducted in Tasmania estimated the inpatient costs of SG (AUD $6,392 per episode and $34,754 per person) was considerably lower than the estimated inpatient costs of LAGB ($7,892 per episode and $61,382 per person) due to LAGB implant-related costs (289). Although SG sample size was relatively low in this study, it does suggest that the Tasmanian Public Hospital system might save on costs if SG is substituted for LAGB when clinically appropriate (289).

- Biliopancreatic diversion (with or without duodenal switch)

We found limited cost effectiveness data on Biliopancreatic diversion (with or without duodenal switch; BPD/DS). Reports show that this procedure is the most costly of the bariatric procedures, but it is also the most effective for obesity management (290). Based on data modelled across all BMI categories using a 10-year horizon, BPD/DS had ICERs of $46,508 USD and $77,574 when compared to standard care and RYGB, respectively (290). Depending on an accepted willingness to pay threshold, this might or may not be considered a cost-effective therapy.

Endoscopic therapies

- Endoscopic sleeve gastroplasty

In a recent cost effectiveness analysis using a state-transition semi-Markov microsimulation model, it was found that ESG is cost effective for people with class I (ICER USD $4105/QALY), class II (ICER $11,411/QALY) and class III (ICER $8213/QALY) obesity over a 30-year horizon when compared to lifestyle-only treatment (288). In another recent study using a 6-state Markov model, ESG had an ICER of UK £2453/QALY gained over a lifetime horizon when compared to lifestyle treatment alone (280). In that study, ESG was consistently cost effective across a wide range of sensitivity analyses.

- Duodeno-Jejunal Bypass Liner (EndoBarrier)

In a recent cost effectiveness analysis investigating an endoluminal duodenal–jejunal bypass liner intervention in comparison with a combination of conventional therapy in people with obesity and comorbid T2D, it was reported that the treatment was not cost effective for weight loss or glycaemic control, generating an ICER of £147,408 over 2 years (281).

- Intra-gastric Balloon therapy

In a recent cost effectiveness analysis using a Markov microsimulation model, it was found that Procedure-less intragastric balloon (PIGB) was cost effective compared to no treatment, with an ICER of USD $21,711 per QALY gained over a lifetime (279). Moreover, PIGB as a bridge to sleeve gastrectomy produced an ICER of USD $3,781 per QALY gained over a lifetime when compared to no treatment. It was found that PIGB +

	SG dominated SG. However, PIGB was not found to be cost effective compared to bariatric surgery (279). *Summary and implications* Cost effectiveness analyses have consistently modelled bariatric surgery as a cost effective treatment for obesity management when compared to usual care/non-surgical treatments, particularly when a lifetime horizon was used in the analyses. Key types of bariatric surgery, including RYGB, AGB and SG have been shown to be cost effective in studies, although studies suggest that RYGB is the most cost-effective across the broadest model conditions. Given this cost-effectiveness, increasing resourcing for publicly funded access to bariatric surgeries such as RYGB could help to match the current unmet demand for bariatric surgery in eligible Australian patients (291) while providing a highly cost-effective approach to obesity management. While less evidence is currently available on cost-effectiveness of endoscopic therapies, some recent evidence shows ESG to be a cost-effective approach in obesity management.	
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising the patient's awareness of available adjunct treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving bariatric and endoscopic surgical treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with moderate to severe obesity, and clinicians, where it is clinically appropriate.	Acceptability increases where interventions (including adjunct interventions) are individually tailored and culturally appropriate. For example, accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of bariatric and endoscopic surgical treatment interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	**Does not favour either the intervention or the comparison**	**Probably favours the intervention**	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	**Large costs**	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Conditional recommendation for the intervention:
Bariatric surgery interventions may be recommended as part of a comprehensive approach to management of weight-related health and wellbeing.

Consensus statement due to very low certainty of evidence:
Some endoscopic therapies may be considered as part of a comprehensive approach to management of weight-related health and wellbeing.

Conditional recommendation for the intervention:
Adjunct therapy combined with bariatric surgery interventions may be recommended as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
2. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
3. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
4. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
5. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
7. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
8. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
9. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
10. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
11. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
12. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
13. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
14. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
15. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119

16. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
17. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
18. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
19. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
20. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
21. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
22. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
23. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
24. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
25. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
26. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
27. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
28. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
29. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
30. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
31. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
32. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
33. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
34. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
35. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
36. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
37. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
38. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157

39. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
40. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
41. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
42. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
43. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
44. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
45. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
46. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
47. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
48. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
49. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
50. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
51. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
52. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
53. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
54. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
55. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
56. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
57. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
58. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
59. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
60. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
61. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
62. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
63. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
64. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085

65. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
66. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
67. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
68. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
69. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
70. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
71. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
72. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
73. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
74. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
75. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
76. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
77. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
78. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
79. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
80. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
81. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
82. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
83. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
84. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
85. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
86. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
87. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
88. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005

89. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
90. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
91. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
92. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
93. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
94. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
95. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
96. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
97. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
98. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
99. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
100. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
101. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
102. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
103. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
104. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
105. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
106. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
107. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
108. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
109. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
110. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
111. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
112. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
113. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393

114. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
115. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
116. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
117. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
118. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
119. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
120. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
121. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
122. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
123. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
124. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
125. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
126. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
127. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
128. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
129. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
130. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
131. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
132. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
133. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
134. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
135. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
136. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
137. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618

138. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
139. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
140. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
141. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
142. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
143. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
144. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
145. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
146. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
147. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
148. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
149. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
150. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
151. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
152. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
153. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
154. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
155. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
156. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
157. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
158. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
159. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
160. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
161. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
162. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
163. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107

164. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
165. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
166. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
167. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
168. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
169. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
170. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
171. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
172. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
173. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
174. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
175. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
176. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
177. Cheng A, Yeoh E, Moh A, Low S, Tan CH, Lam B, et al. Roux-en-Y gastric bypass versus best medical treatment for type 2 diabetes mellitus in adults with body mass index between 27 and 32 kg/m2: a 5-year randomized controlled trial. Diabetes Res Clin Pract. 2022;188:109900. doi: 10.1016/j.diabres.2022.109900
178. Courcoulas AP, Gallagher JW, Neiberg RH, Eagleton EB, DeLany JP, Lang W, et al. Bariatric surgery vs lifestyle intervention for diabetes treatment: 5-year outcomes from a randomized trial. J Clin Endocrinol Metab. 2020;105(3):866–76. doi: 10.1210/clinem/dgaa006
179. Cummings DE, Arterburn DE, Westbrook EO, Kuzma JN, Stewart SD, Chan CP, et al. Gastric bypass surgery vs intensive lifestyle and medical intervention for type 2 diabetes: the CROSSROADS randomised controlled trial. Diabetologia. 2016;59(5):945-53. doi: 10.1007/s00125-016-3903-x
180. Dowsey MM, Brown WA, Cochrane A, Burton PR, Liew D, Choong PF. Effect of bariatric surgery on risk of complications after total knee arthroplasty: a randomized clinical trial. JAMA Netw Open. 2022;5(4):e226722. doi: 10.1001/jamanetworkopen.2022.6722
181. Feigel-Guiller B, Drui D, Dimet J, Zair Y, Le Bras M, Fuertes-Zamorano N, et al. Laparoscopic gastric banding in obese patients with sleep apnea: a 3-year controlled study and follow-up after 10 years. Obes Surg. 2015;25(10):1886-92. doi: 10.1007/s11695-015-1627-5
182. Ikramuddin S, Billington CJ, Lee W-J, Bantle JP, Thomas AJ, Connett JE, et al. Roux-en-Y gastric bypass for diabetes (the Diabetes Surgery Study): 2-year outcomes of a 5-year, randomised, controlled trial. Lancet Diabetes Endocrinol. 2015;3(6):413-22. doi: 10.1016/S2213-8587(15)00089-3
183. Ikramuddin S, Korner J, Lee W-J, Bantle JP, Thomas AJ, Connett JE, et al. Durability of addition of Roux-en-Y gastric bypass to lifestyle intervention and medical management in achieving primary treatment goals for uncontrolled type 2 diabetes in mild to moderate obesity: a randomized control trial. Diabetes Care. 2016;39(9):1510-8. doi: 10.2337/dc15-2481
184. Ikramuddin S, Korner J, Lee W-J, Connett JE, Inabnet WB, Billington CJ, et al. Roux-en-Y gastric bypass vs intensive medical management for the control of type 2 diabetes, hypertension, and hyperlipidemia: the Diabetes Surgery Study randomized clinical trial. JAMA. 2013;309(21):2240-9. doi: 10.1001/jama.2013.5835
185. Koschker A-C, Warrings B, Morbach C, Seyfried F, Jung P, Dischinger U, et al. Effect of bariatric surgery on cardio-psycho-metabolic outcomes in severe obesity: a randomized controlled trial. Metabolism. 2023;147:155655. doi: 10.1016/j.metabol.2023.155655

186. Maghrabi AH, Wolski K, Abood B, Licata A, Pothier C, Bhatt DL, et al. Two-year outcomes on bone density and fracture incidence in patients with T2DM randomized to bariatric surgery versus intensive medical therapy. Obesity. 2015;23(12):2344-8. doi: 10.1002/oby.21150
187. Ospanov O, Akilzhanova A, Buchwald JN, Fursov A, Bekmurzinova F, Rakhimova S, et al. Stapleless vs stapled gastric bypass vs yypocaloric diet: a three-arm randomized controlled trial of body mass evolution with secondary outcomes for telomere length and metabolic syndrome changes. Obes Surg. 2021;31(7):3165-76. doi: 10.1007/s11695-021-05454-2
188. Schauer PR, Kashyap SR, Wolski K, Brethauer SA, Kirwan JP, Pothier CE, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med. 2012;366(17):1567-76. doi: 10.1056/NEJMoa1200225
189. Schiavon CA, Bersch-Ferreira AC, Santucci EV, Oliveira JD, Torreglosa CR, Bueno PT, et al. Effects of bariatric surgery in obese patients with hypertension: the GATEWAY randomized Trial (Gastric Bypass to Treat Obese Patients With Steady Hypertension). Circulation. 2018;137(11):1132-42. doi: 10.1161/CIRCULATIONAHA.117.032130
190. Simonson DC, Halperin F, Foster K, Vernon A, Goldfine AB. Clinical and patient-centered outcomes in obese patients with type 2 diabetes 3 years after randomization to Roux-en-Y gastric bypass surgery versus intensive lifestyle management: the SLIMM-T2D study. Diabetes Care. 2018;41(4):670-9. doi: 10.2337/dc17-0487
191. Simonson DC, Vernon A, Foster K, Halperin F, Patti ME, Goldfine AB. Adjustable gastric band surgery or medical management in patients with type 2 diabetes and obesity: three-year results of a randomized trial. Surg Obes Relat Dis. 2019;15(12):2052-9. doi: 10.1016/j.soard.2019.03.038
192. Verrastro O, Panunzi S, Castagneto-Gissey L, De Gaetano A, Lembo E, Capristo E, et al. Bariatric-metabolic surgery versus lifestyle intervention plus best medical care in non-alcoholic steatohepatitis (BRAVES): a multicentre, open-label, randomised trial. Lancet. 2023;401(10390):1786-97. doi: 10.1016/S0140-6736(23)00634-7
193. Abu Dayyeh BK, Bazerbachi F, Vargas EJ, Sharaiha RZ, Thompson CC, Thaemert BC, et al. Endoscopic sleeve gastroplasty for treatment of class 1 and 2 obesity (MERIT): a prospective, multicentre, randomised trial. Lancet. 2022;400(10350):441-51. doi: 10.1016/S0140-6736(22)01280-6
194. Caiazzo R, Branche J, Raverdy V, Czernichow S, Carette C, Robert M, et al. Efficacy and safety of the duodeno-jejunal bypass liner in patients with metabolic syndrome: a multicenter randomized controlled trial (ENDOMETAB). Ann Surg. 2020;272(5):696-702. doi: 10.1097/SLA.0000000000004339
195. Glaysher MA, Ward J, Aldhwayan M, Ruban A, Prechtl CG, Fisk HL, et al. The effect of a duodenal-jejunal bypass liner on lipid profile and blood concentrations of long chain polyunsaturated fatty acids. Clin Nutr. 2021;40(4):2343-54. doi: 10.1016/j.clnu.2020.10.026
196. Gómez V, Woodman G, Abu Dayyeh BK. Delayed gastric emptying as a proposed mechanism of action during intragastric balloon therapy: results of a prospective study. Obesity. 2016;24(9):1849-53. doi: 10.1002/oby.21555
197. Koehestanie P, de Jonge C, Berends FJ, Janssen IM, Bouvy ND, Greve JWM. The effect of the endoscopic duodenal-jejunal bypass liner on obesity and type 2 diabetes mellitus, a multicenter randomized controlled trial. Ann Surg. 2014;260(6):984-92. doi: 10.1097/SLA.0000000000000794
198. Miller K, Turró R, Greve JW, Bakker CM, Buchwald JN, Espinos JC. MILEPOST multicenter randomized controlled trial: 12-month weight loss and satiety outcomes after *pose* SM vs. medical therapy. Obes Surg. 2017;27(2):310-22. doi: 10.1007/s11695-016-2295-9
199. Sullivan S, Swain JM, Woodman G, Antonetti M, De La Cruz-Muñoz N, Jonnalagadda SS, et al. Randomized sham-controlled trial evaluating efficacy and safety of endoscopic gastric plication for primary obesity: the ESSENTIAL trial. Obesity. 2017;25(2):294-301. doi: 10.1002/oby.21702
200. Thompson CC, Abu Dayyeh BK, Kushner R, Sullivan S, Schorr AB, Amaro A, et al. Percutaneous gastrostomy device for the treatment of class II and class III obesity: results of a randomized controlled trial. Am J Gastroenterol. 2017;112(3):447-57. doi: 10.1038/ajg.2016.500
201. Chan DL, Cruz JR, Mui WL, Wong SKH, Ng EKW. Outcomes with intra-gastric balloon therapy in BMI < 35 non-morbid obesity: 10-year follow-up study of an RCT. Obes Surg. 2021;31(2):781-6. doi: 10.1007/s11695-020-04986-3
202. Baillot A, Vallée C-A, Mampuya WM, Dionne IJ, Comeau E, Méziat-Burdin A, Langlois M-F. Effects of a pre-surgery supervised exercise training 1 year after bariatric surgery: a randomized controlled study. Obes Surg. 2018;28(4):955-62. doi: 10.1007/s11695-017-2943-8
203. Versteegden DPA, Van Himbeeck MJJ, Luyer MD, van Montfort G, de Zoete J-PJGM, Smulders JF, Nienhuijs SW. A randomized clinical trial evaluating eHealth in bariatric surgery. Surg Endosc. 2023;37(10):7625-33. doi: 10.1007/s00464-023-10211-w
204. Belzile D, Auclair A, Roberge J, Piché ME, Lebel A, Pettigrew M, et al. Heart rate variability after bariatric surgery: the add-on value of exercise. Eur J Sport Sci. 2023;23(3):415-22. doi: 10.1080/17461391.2021.2017488
205. Lier HØ, Biringer E, Stubhaug B, Tangen T. The impact of preoperative counseling on postoperative treatment adherence in bariatric surgery patients: a randomized controlled trial. Patient Educ Couns. 2012;87(3):336-42. doi: 10.1016/j.pec.2011.09.014
206. Chandrakumar H, Khatun N, Gupta T, Graham-Hill S, Zhyvotovska A, McFarlane SI. The effects of bariatric Surgery on cardiovascular outcomes and cardiovascular mortality: a systematic review and meta-analysis. Cureus. 2023;15(2):e34723. doi: 10.7759/cureus.34723
207. Pontiroli AE, Centofanti L, Le Roux CW, Magnani S, Tagliabue E, Folli F. Effect of prolonged and substantial weight loss on incident atrial fibrillation: a systematic review and meta-analysis. Nutrients. 2023;15(4):940. doi: 10.3390/nu15040940

208. Tang B, Zhang Y, Wang Y, Wang X, An Z, Yu X. Effect of bariatric surgery on long-term cardiovascular outcomes: a systematic review and meta-analysis of population-based cohort studies. Surg Obes Relat Dis. 2022;18(8):1074-86. doi: 10.1016/j.soard.2022.05.007
209. Wiggins T, Guidozzi N, Welbourn R, Ahmed AR, Markar SR. Association of bariatric surgery with all-cause mortality and incidence of obesity-related disease at a population level: a systematic review and meta-analysis. PLoS Med. 2020;17(7):e1003206. doi: 10.1371/journal.pmed.1003206
210. Colquitt JL, Pickett K, Loveman E, Frampton GK. Surgery for weight loss in adults. Cochrane Database Syst Rev. 2014(8):CD003641. doi: 10.1002/14651858.CD003641.pub4
211. Wang G, Huang Y, Yang H, Lin H, Zhou S, Qian J. Impacts of bariatric surgery on adverse liver outcomes: a systematic review and meta-analysis. Surg Obes Relat Dis. 2023;19(7):717-26. doi: 10.1016/j.soard.2022.12.025
212. Groen VA, van de Graaf VA, Scholtes VAB, Sprague S, van Wagensveld BA, Poolman RW. Effects of bariatric surgery for knee complaints in (morbidly) obese adult patients: a systematic review. Obes Rev. 2015;16(2):161-70. doi: 10.1111/obr.12236
213. Wilson RB, Lathigara D, Kaushal D. Systematic review and meta-analysis of the impact of bariatric surgery on future cancer risk. Int J Mol Sci. 2023;24(7). doi: 10.3390/ijms24076192
214. Driscoll S, Gregory DM, Fardy JM, Twells LK. Long-term health-related quality of life in bariatric surgery patients: a systematic review and meta-analysis. Obesity. 2016;24(1):60-70. doi: 10.1002/oby.21322
215. Wang L, Lin M, Yu J, Fan Z, Zhang S, Lin Y, et al. The impact of bariatric surgery versus non-surgical treatment on blood pressure: systematic review and meta-analysis. Obes Surg. 2021;31(11):4970-84. doi: 10.1007/s11695-021-05671-9
216. Cohen R, Sforza NS, Clemente RG. Impact of metabolic surgery on type 2 diabetes mellitus, cardiovascular risk factors, and mortality: a review. Curr Hypertens Rev. 2021;17(2):159-69. doi: 10.2174/1573402116666200804153228
217. Cheng J, Gao J, Shuai X, Wang G, Tao K. The comprehensive summary of surgical versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomized controlled trials. Oncotarget. 2016;7(26):39216-30. doi: 10.18632/oncotarget.9581
218. Zhou X, Zeng C. Diabetes remission of bariatric surgery and nonsurgical treatments in type 2 diabetes patients who failure to meet the criteria for surgery: a systematic review and meta-analysis. BMC Endocr Disord. 2023;23(1):46. doi: 10.1186/s12902-023-01283-9
219. Sheng B, Truong K, Spitler H, Zhang L, Tong X, Chen L. The long-term effects of bariatric surgery on type 2 diabetes remission, microvascular and macrovascular complications, and mortality: a systematic review and meta-analysis. Obes Surg. 2017;27(10):2724-32. doi: 10.1007/s11695-017-2866-4
220. Hussain S, Khan MS, Jamali MC, Siddiqui AN, Gupta G, Hussain MS, Husain FM. Impact of bariatric surgery in reducing macrovascular complications in severely obese T2DM patients. Obes Surg. 2021;31(5):1929-36. doi: 10.1007/s11695-020-05155-2
221. Meijer RI, van Wagensveld BA, Siegert CE, Eringa EC, Serné EH, Smulders YM. Bariatric surgery as a novel treatment for type 2 diabetes mellitus: a systematic review. Arch Surg. 2011;146(6):744-50. doi: 10.1001/archsurg.2011.134
222. De Luca M, Zese M, Bandini G, Chiappetta S, Iossa A, Merola G, et al. Metabolic bariatric surgery as a therapeutic option for patients with type 2 diabetes: a meta-analysis and network meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2023;25(8):2362-73. doi: 10.1111/dom.15117
223. Li Y, Gu Y, Jin Y, Mao Z. Is bariatric surgery effective for Chinese patients with type 2 diabetes mellitus and body mass index < 35 kg/m2? A systematic review and meta-analysis. Obes Surg. 2021;31(9):4083-92. doi: 10.1007/s11695-021-05520-9
224. Athanasiadis DI, Martin A, Kapsampelis P, Monfared S, Stefanidis D. Factors associated with weight regain post-bariatric surgery: a systematic review. Surg Endosc. 2021;35(8):4069-84. doi: 10.1007/s00464-021-08329-w
225. Blaine B, Rodman J. Responses to weight loss treatment among obese individuals with and without BED: a matched-study meta-analysis. Eat Weight Disord. 2007;12(2):54-60. doi: 10.1007/BF03327579
226. Blaine BE, Rodman J, Newman JM. Weight loss treatment and psychological well-being: a review and meta-analysis. J Health Psychol. 2007;12(1):66-82. doi: 10.1177/1359105307071741
227. David LA, Sijercic I, Cassin SE. Preoperative and post-operative psychosocial interventions for bariatric surgery patients: a systematic review. Obes Rev. 2020;21(4):e12926. doi: 10.1111/obr.12926
228. Fu R, Zhang Y, Yu K, Mao D, Su H. Bariatric surgery alleviates depression in obese patients: a systematic review and meta-analysis. Obes Res Clin Pract. 2022;16(1):10-6. doi: 10.1016/j.orcp.2021.11.002
229. Gill H, Kang S, Lee Y, Rosenblat JD, Brietzke E, Zuckerman H, McIntyre RS. The long-term effect of bariatric surgery on depression and anxiety. J Affect Disord. 2019;246:886-94. doi: 10.1016/j.jad.2018.12.113
230. Seyhan Ak E, Aci ÖS, Kutlu FY. Obezite Cerrahisi Öncesinde ve İyileşme Sürecinde Psikososyal Girişimler: Sistematik Literatür İncelemesi. Turkiye Klinikleri J Nurs Sci. 2020;12(4):625-32. doi: 10.5336/nurses.2020-75307
231. Loh HH, Francis B, Lim L-L, Lim QH, Yee A, Loh HS. Improvement in mood symptoms after post-bariatric surgery among people with obesity: a systematic review and meta-analysis. Diabetes Metab Res Rev. 2021;37(8):e3458. doi: 10.1002/dmrr.3458
232. Marshall S, Mackay H, Matthews C, Maimone IR, Isenring E. Does intensive multidisciplinary intervention for adults who elect bariatric surgery improve post-operative weight loss, co-morbidities, and quality of life? A systematic review and meta-analysis. Obes Rev. 2020;21(7):e13012. doi: 10.1111/obr.13012

233. Opozda M, Chur-Hansen A, Wittert G. Changes in problematic and disordered eating after gastric bypass, adjustable gastric banding and vertical sleeve gastrectomy: a systematic review of pre-post studies. Obes Rev. 2016;17(8):770-92. doi: 10.1111/obr.12425
234. Taba JV, Suzuki MO, Nascimento FSd, Iuamoto LR, Hsing WT, Pipek LZ, et al. The development of feeding and eating disorders after bariatric surgery: a systematic review and meta-analysis. Nutrients. 2021;13(7). doi: 10.3390/nu13072396
235. Ansari M, Serjeant S. Patient experiences of weight loss and eating after bariatric surgery: a systematic review and qualitative synthesis. J Hum Nutr Diet. 2023;36(4):1438-50. doi: 10.1111/jhn.13121
236. Cohn I, Raman J, Sui Z. Patient motivations and expectations prior to bariatric surgery: a qualitative systematic review. Obes Rev. 2019;20(11):1608-18. doi: 10.1111/obr.12919
237. Coulman KD, MacKichan F, Blazeby JM, Owen-Smith A. Patient experiences of outcomes of bariatric surgery: a systematic review and qualitative synthesis. Obes Rev. 2017;18(5):547-59. doi: 10.1111/obr.12518
238. Herpertz S, Kielmann R, Wolf AM, Langkafel M, Senf W, Hebebrand J. Does obesity surgery improve psychosocial functioning? A systematic review. Int J Obes. 2003;27(11):1300-14. doi: 10.1038/sj.ijo.0802410
239. Doni K, Breuing J, Pieper D. Psychosocial changes of bariatric surgery in patients' everyday life: a scoping review. Obes Surg. 2020;30(8):2949-56. doi: 10.1007/s11695-020-04621-1
240. Pietrabissa G, Bertuzzi V, Simpson S, Guerrini Usubini A, Cattivelli R, Bertoli S, et al. Psychological aspects of treatment with intragastric balloon for management of obesity: a systematic review of the literature. Obes Facts. 2022;15(1):1-18. doi: 10.1159/000518200
241. Cheroutre C, Guerrien A, Rousseau A. Contributing of cognitive-behavioral therapy in the context of bariatric surgery: a review of the literature. Obes Surg. 2020;30(8):3154-66. doi: 10.1007/s11695-020-04627-9
242. Er E, Durieux N, Vander Haegen M, Flahault C, Etienne A-M. Patients' perceptions of the mechanisms underlying alcohol use problems after bariatric surgery: a qualitative systematic review. Clin Obes. 2023;13(1):e12551. doi: 10.1111/cob.12551
243. Layton GR, Bhanderi S, Sahloul M, Charalampakis V, Daskalakis M, Singhal R. Challenges and outcomes for bariatric surgery in patients with paraplegia: case series and systematic review. Clin Obes. 2020;10(4):e12382. doi: 10.1111/cob.12382
244. Li Z, Pan Y, Zhang Y, Qin J, Lei X. Dietary experiences after bariatric surgery in patients with obesity: a qualitative systematic review. Obes Surg. 2022;32(6):2023-34. doi: 10.1007/s11695-022-06018-8
245. Bonn SE, Hult M, Spetz K, Eke H, Andersson E, Wirén M, et al. Effect of a smartphone application on physical activity and weight loss after bariatric surgery-results from a randomized controlled trial. Obes Surg. 2023;33(9):2841-50. doi: 10.1007/s11695-023-06753-6
246. Fagevik Olsén M, Wiklund M, Sandberg E, Lundqvist S, Dean E. Long-term effects of physical activity prescription after bariatric surgery: a randomized controlled trial. Physiother Theory Pract. 2022;38(11):1591-601. doi: 10.1080/09593985.2021.1885087
247. Hjelmesæth J, Rosenvinge JH, Gade H, Friborg O. Effects of cognitive behavioral therapy on eating behaviors, affective symptoms, and weight loss after bariatric surgery: a randomized clinical trial. Obes Surg. 2019;29(1):61-9. doi: 10.1007/s11695-018-3471-x
248. Ogden J, Hollywood A, Pring C. The impact of psychological support on weight loss post weight loss surgery: a randomised control trial. Obes Surg. 2015;25(3):500-5. doi: 10.1007/s11695-014-1428-2
249. Paul L, van der Heiden C, van Hoeken D, Deen M, Vlijm A, Klaassen R, et al. Three- and five-year follow-up results of a randomized controlled trial on the effects of cognitive behavioral therapy before bariatric surgery. Int J Eat Disord. 2022;55(12):1824-37. doi: 10.1002/eat.23825
250. Wild B, Hünnemeyer K, Sauer H, Hain B, Mack I, Schellberg D, et al. A 1-year videoconferencing-based psychoeducational group intervention following bariatric surgery: results of a randomized controlled study. Surg Obes Relat Dis. 2015;11(6):1349-60. doi: 10.1016/j.soard.2015.05.018
251. Gade H, Friborg O, Rosenvinge JH, Småstuen MC, Hjelmesæth J. The impact of a preoperative cognitive behavioural therapy (CBT) on dysfunctional eating behaviours, affective symptoms and body weight 1 year after bariatric surgery: a randomised controlled trial. Obes Surg. 2015;25(11):2112-9. doi: 10.1007/s11695-015-1673-z
252. Lovrics O, Butt J, Lee Y, Lovrics P, Boudreau V, Anvari M, et al. The effect of bariatric surgery on breast cancer incidence and characteristics: a meta-analysis and systematic review. Am J Surg. 2021;222(4):715-22. doi: 10.1016/j.amjsurg.2021.03.016
253. Lee S-Y, Lai H, Chua YJ, Wang MX, Lee G-H. Endoscopic bariatric and metabolic therapies and their effects on metabolic syndrome and non-alcoholic fatty liver disease - a systematic review and meta-analysis. Front Med (Lausanne). 2022;9:880749. doi: 10.3389/fmed.2022.880749
254. Gloy VL, Briel M, Bhatt DL, Kashyap SR, Schauer PR, Mingrone G, et al. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. BMJ. 2013;347:f5934. doi: 10.1136/bmj.f5934
255. Baillot A, Brais-Dussault E, Bastin A, Cyr C, Brunet J, Aimé A, et al. What is known about the correlates and impact of excess skin after bariatric surgery: a scoping review. Obes Surg. 2017;27(9):2488-98. doi: 10.1007/s11695-017-2814-3
256. Mori C, Sheehan D, Graor CH, Petrinec A. A scoping review of the phenomenon of osteoporosis in post bariatric surgical patients. Int J Orthop Trauma Nurs. 2021;40:100835. doi: 10.1016/j.ijotn.2020.100835
257. Castaneda D, Popov VB, Wander P, Thompson CC. Risk of suicide and self-harm is increased after bariatric surgery-a systematic review and meta-analysis. Obes Surg. 2019;29(1):322-33. doi: 10.1007/s11695-018-3493-4

258. Van den Eynde A, Mertens A, Vangoitsenhoven R, Meulemans A, Matthys C, Deleus E, et al. Psychosocial consequences of bariatric surgery: two sides of a coin: a scoping review. Obes Surg. 2021;31(12):5409-17. doi: 10.1007/s11695-021-05674-6
259. Hung A, Maciejewski ML, Berkowitz TSZ, Arterburn DE, Mitchell JE, Bradley KA, et al. Bariatric Surgery and Suicide Risk in Patients With Obesity. Ann Surg. 2023;278(4):e760-e5. doi: 10.1097/sla.0000000000005825
260. Borisenko O, Adam D, Funch-Jensen P, Ahmed AR, Zhang R, Colpan Z, Hedenbro J. Bariatric Surgery can Lead to Net Cost Savings to Health Care Systems: Results from a Comprehensive European Decision Analytic Model. Obes Surg. 2015;25(9):1559-68. doi: 10.1007/s11695-014-1567-5
261. Borisenko O, Lukyanov V, Ahmed AR. Cost-utility analysis of bariatric surgery. Br J Surg. 2018;105(10):1328-37. doi: 10.1002/bjs.10857
262. Borisenko O, Lukyanov V, Debergh I, Dillemans B. Cost-effectiveness analysis of bariatric surgery for morbid obesity in Belgium. J Med Econ. 2018;21(4):365-73. doi: 10.1080/13696998.2017.1419958
263. Borisenko O, Lukyanov V, Johnsen SP, Funch-Jensen P. Cost analysis of bariatric surgery in Denmark made with a decision-analytic model. Dan Med J. 2017;64(8).
264. Borisenko O, Mann O, Duprée A. Cost-utility analysis of bariatric surgery compared with conventional medical management in Germany: a decision analytic modeling. BMC Surg. 2017;17(1):87. doi: 10.1186/s12893-017-0284-0
265. Castilla I, Mar J, Valcárcel-Nazco C, Arrospide A, Ramos-Goñi JM. Cost-utility analysis of gastric bypass for severely obese patients in Spain. Obes Surg. 2014;24(12):2061-8. doi: 10.1007/s11695-014-1304-0
266. Faria GR, Preto JR, Costa-Maia J. Gastric bypass is a cost-saving procedure: results from a comprehensive Markov model. Obes Surg. 2013;23(4):460-6. doi: 10.1007/s11695-012-0816-8
267. Gulliford MC, Charlton J, Prevost T, Booth H, Fildes A, Ashworth M, et al. Costs and Outcomes of Increasing Access to Bariatric Surgery: Cohort Study and Cost-Effectiveness Analysis Using Electronic Health Records. Value Health. 2017;20(1):85-92. doi: 10.1016/j.jval.2016.08.734
268. James R, Salton RI, Byrnes JM, Scuffham PA. Cost-utility analysis for bariatric surgery compared with usual care for the treatment of obesity in Australia. Surg Obes Relat Dis. 2017;13(12):2012-20. doi: 10.1016/j.soard.2016.12.016
269. Lucchese M, Borisenko O, Mantovani LG, Cortesi PA, Cesana G, Adam D, et al. Cost-Utility Analysis of Bariatric Surgery in Italy: Results of Decision-Analytic Modelling. Obes Facts. 2017;10(3):261-72. doi: 10.1159/000475842
270. Mäklin S, Malmivaara A, Linna M, Victorzon M, Koivukangas V, Sintonen H. Cost-utility of bariatric surgery for morbid obesity in Finland. Br J Surg. 2011;98(10):1422-9. doi: 10.1002/bjs.7640
271. McEwen LN, Coelho RB, Baumann LM, Bilik D, Nota-Kirby B, Herman WH. The cost, quality of life impact, and cost-utility of bariatric surgery in a managed care population. Obes Surg. 2010;20(7):919-28. doi: 10.1007/s11695-010-0169-0
272. Lester ELW, Padwal RS, Birch DW, Sharma AM, So H, Ye F, Klarenbach SW. The real-world cost-effectiveness of bariatric surgery for the treatment of severe obesity: a cost-utility analysis. CMAJ Open. 2021;9(2):E673-e9. doi: 10.9778/cmajo.20200188
273. Alsumali A, Eguale T, Bairdain S, Samnaliev M. Cost-Effectiveness Analysis of Bariatric Surgery for Morbid Obesity. Obes Surg. 2018;28(8):2203-14. doi: 10.1007/s11695-017-3100-0
274. Assumpção RP, Bahia LR, da Rosa MQM, Correia MG, da Silva EN, Zubiaurre PR, et al. Cost-Utility of Gastric Bypass Surgery Compared to Clinical Treatment for Severely Obese With and Without Diabetes in the Perspective of the Brazilian Public Health System. Obes Surg. 2019;29(10):3202-11. doi: 10.1007/s11695-019-03957-7
275. Boyers D, Retat L, Jacobsen E, Avenell A, Aveyard P, Corbould E, et al. Cost-effectiveness of bariatric surgery and non-surgical weight management programmes for adults with severe obesity: a decision analysis model. Int J Obes. 2021;45(10):2179-90. doi: 10.1038/s41366-021-00849-8
276. Campbell J, McGarry LA, Shikora SA, Hale BC, Lee JT, Weinstein MC. Cost-effectiveness of laparoscopic gastric banding and bypass for morbid obesity. Am J Manag Care. 2010;16(7):e174-87.
277. Craig BM, Tseng DS. Cost-effectiveness of gastric bypass for severe obesity. Am J Med. 2002;113(6):491-8. doi: 10.1016/s0002-9343(02)01266-4
278. Keating CL, Dixon JB, Moodie ML, Peeters A, Bulfone L, Maglianno DJ, O'Brien PE. Cost-effectiveness of surgically induced weight loss for the management of type 2 diabetes: modeled lifetime analysis. Diabetes Care. 2009;32(4):567-74. doi: 10.2337/dc08-1749
279. Mital S, Nguyen HV. Cost-effectiveness of procedure-less intragastric balloon therapy as substitute or complement to bariatric surgery. PLoS ONE. 2021;16(7):e0254063. doi: 10.1371/journal.pone.0254063
280. Kelly J, Menon V, O'Neill F, Elliot L, Combe E, Drinkwater W, et al. UK cost-effectiveness analysis of endoscopic sleeve gastroplasty versus lifestyle modification alone for adults with class II obesity. Int J Obes. 2023;47(11):1161-70. doi: 10.1038/s41366-023-01374-6
281. Ruban A, Glaysher MA, Miras AD, Goldstone AP, Prechtl CG, Johnson N, et al. Efficacy and Mechanism Evaluation. A duodenal sleeve bypass device added to intensive medical therapy for obesity with type 2 diabetes: a RCT. Southampton (UK): NIHR Journals Library; 2020.
282. Augustovski F, Colantonio LD, Galante J, Bardach A, Caporale JE, Zárate V, et al. Measuring the Benefits of Healthcare: DALYs and QALYs - Does the Choice of Measure Matter? A Case Study of Two Preventive Interventions. Int J Health Policy Manag. 2018;7(2):120-36. doi: 10.15171/ijhpm.2017.47

283. Noparatayaporn P, Thavorncharoensap M, Chaikledkaew U, Bagepally BS, Thakkinstian A. Incremental Net Monetary Benefit of Bariatric Surgery: Systematic Review and Meta-Analysis of Cost-Effectiveness Evidences. Obes Surg. 2021;31(7):3279-90. doi: 10.1007/s11695-021-05415-9
284. Sanchez-Santos R, Padin EM, Adam D, Borisenko O, Fernandez SE, Dacosta EC, et al. Bariatric surgery versus conservative management for morbidly obese patients in Spain: a cost-effectiveness analysis. Expert Rev Pharmacoecon Outcomes Res. 2018;18(3):305-14. doi: 10.1080/14737167.2018.1407649
285. Jordan K, Fawsitt CG, Carty PG, Clyne B, Teljeur C, Harrington P, Ryan M. Cost-effectiveness of metabolic surgery for the treatment of type 2 diabetes and obesity: a systematic review of economic evaluations. Eur J Health Econ. 2023;24(4):575-90. doi: 10.1007/s10198-022-01494-2
286. Lauren BN, Lim F, Krikhely A, Taveras EM, Woo Baidal JA, Bellows BK, Hur C. Estimated Cost-effectiveness of Medical Therapy, Sleeve Gastrectomy, and Gastric Bypass in Patients With Severe Obesity and Type 2 Diabetes. JAMA Netw Open. 2022;5(2):e2148317. doi: 10.1001/jamanetworkopen.2021.48317
287. Wang BC, Wong ES, Alfonso-Cristancho R, He H, Flum DR, Arterburn DE, et al. Cost-effectiveness of bariatric surgical procedures for the treatment of severe obesity. Eur J Health Econ. 2014;15(3):253-63. doi: 10.1007/s10198-013-0472-5
288. Saumoy M, Gandhi D, Buller S, Patel S, Schneider Y, Cote G, et al. Cost-effectiveness of endoscopic, surgical and pharmacological obesity therapies: a microsimulation and threshold analyses. Gut. 2023;72(12):2250-9. doi: 10.1136/gutjnl-2023-330437
289. Campbell JA, Hensher M, Davies D, Green M, Hagan B, Jordan I, et al. Long-Term Inpatient Hospital Utilisation and Costs (2007-2008 to 2015-2016) for Publicly Waitlisted Bariatric Surgery Patients in an Australian Public Hospital System Based on Australia's Activity-Based Funding Model. Pharmacoecon Open. 2019;3(4):599-618. doi: 10.1007/s41669-019-0140-5
290. Institute for Clinical and Economic Review. Bariatric surgery final evidence report. Washington State health Care Authority; 2015.
291. Dona SWA, Angeles MR, Nguyen D, Gao L, Hensher M. Obesity and Bariatric Surgery in Australia: Future Projection of Supply and Demand, and Costs. Obes Surg. 2022;32(9):3013-22. doi: 10.1007/s11695-022-06188-5

Question: Surgical interventions compared to treated/untreated comparators for weight maintenance/loss in young and middle-aged adults experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	surgical interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Bariatric surgery intervention vs best medical treatment (baseline to 12 months)												
16[a]	randomised trials	serious[b]	very serious[c]	not serious	not serious	publication bias strongly suspected very strong association[d]	734	567	-	Hedges' g **1.92 lower** (2.32 lower to 1.52 lower)	⨁⨁◯◯ Low	Bariatric surgery interventions may result in a large reduction in adiposity
Laparoscopic adjustable gastric banding (LAGB) versus best medical treatment (baseline to 12 months)												
5[e]	randomised trials	serious[f]	very serious[g]	not serious	serious[h]	very strong association	125	132	-	Hedges' g **1.33 lower** (2.3 lower to 0.36 lower)	⨁⨁◯◯ Low	Laparoscopic adjustable gastric banding (LAGB) may result in a large reduction in adiposity
Roux-en-**Y Gastric Bypass (RYGB) surgery versus best medical treatment (baseline to 12 months)**												
11[i]	randomised trials	serious[j]	very serious[k]	not serious	not serious	publication bias strongly suspected very strong association[l]	442	435	-	Hedges' g **2.2 lower** (2.63 lower to 1.76 lower)	⨁⨁◯◯ Low	Roux-en-Y Gastric Bypass (RYGB) surgery may result in a large reduction in adiposity
Sleeve Gastrectomy (SG) versus best medical treatment (baseline to 12 months)												
3[m]	randomised trials	serious[n]	very serious[o]	not serious	serious[p]	very strong association	147	138	-	Hedges' g **2.18 lower** (4.82 lower to 0.46 higher)	⨁⨁◯◯ Low	Sleeve Gastrectomy (SG) may result in a large reduction in adiposity
Stapled laparoscopic mini-gastric bypass-one anastomosis gastric bypass (LMGB-OAGB) versus best medical treatment (baseline to 12 months)												
1[q]	randomised trials	not serious	not serious	not serious	very serious[r]	very strong association	1/1 study found a positive effect of stapled laparoscopic mini-gastric bypass-one anastomosis gastric bypass (LMGB-OAGB) on weight maintenance/loss. BMI decreased by 16.04kg/m^2 in the intervention group versus 2.76kg/m^2 in the comparator group.				⨁⨁⨁⨁ High	Stapled laparoscopic mini-gastric bypass-one anastomosis gastric bypass (LMGB-OAGB) results in a large reduction in adiposity
Endoscopic surgery intervention versus best medical treatment (baseline to 12 months)												
8[s]	randomised trials	very serious[t]	very serious[u]	not serious	not serious	strong association	578	416	-	Hedges' g **0.88 lower** (1.27 lower to 0.49 lower)	⨁◯◯◯ Very low	Bariatric surgery plus adjunct therapy may result in little to no difference in adiposity.
Duodenal-jejunal bypass liner (EndoBarrier) versus best medical treatment (baseline to 12 months)												

3[m]	randomised trials	very serious[v]	not serious	not serious	serious[p]	none	126	112	-	Hedges' g **0.55 lower** (1.19 lower to 0.09 higher)	⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity
g-CathEZ **delivery catheter with snowshoe suture anchors versus best medical treatment (baseline to 12 months)**												
2[w]	randomised trials	serious[x]	not serious	not serious	serious[h]	none	251	120	-	Hedges' g **0.55 lower** (0.77 lower to 0.33 lower)	⊕⊕◯◯ Low	g-CathEZ delivery catheter with snowshoe suture anchors may reduce adiposity
Endoscopic sleeve gastroplasty versus best medical treatment (baseline to 12 months)												
1[q]	randomised trials	very serious[v]	not serious	not serious	serious[h]	very strong association	1/1 study found a positive effect of endoscopic sleeve gastroplasty on weight maintenance/loss. Mean weight loss was 13.4kg in intervention arm versus 0.8kg in the comparator arm				⊕⊕⊕◯ Moderate	Endoscopic sleeve gastroplasty likely results in a large reduction in adiposity
Percutaneous gastrostomy device versus best medical treatment (baseline to 12 months)												
1[q]	randomised trials	serious[x]	not serious	not serious	serious[h]	very strong association	1/1 study found a positive effect of percutaneous gastrostomy device on weight maintenance/loss. Mean weight loss was 14.2kg in the intervention arm versus 4.1kg in the comparator arm.				⊕⊕⊕⊕ High	Percutaneous gastrostomy device results in a large reduction in adiposity
Intragastric balloon therapy versus best medical treatment (baseline to 12 months)												
1[q]	randomised trials	serious[x]	not serious	not serious	very serious[r]	very strong association	1/1 study found a positive effect of intragastric balloon therapy on weight maintenance/loss. Total body weight loss (%) was 10.6% in the intervention arm versus 3.3% in the comparator arm				⊕⊕⊕◯ Moderate	Intragastric balloon therapy likely results in a large reduction in adiposity
Bariatric surgery plus adjunct therapy intervention vs bariatric surgery plus usual care/placebo (baseline to 12 months)												
9[y]	randomised trials	serious[z]	not serious	not serious	serious[aa]	none	472	502	-	Hedges' g **0.04 higher** (0.1 lower to 0.19 higher)	⊕⊕◯◯ Low	Bariatric surgery plus adjunct therapy may result in little to no difference in adiposity.
Biliopancreatic diversion with duodenal switch (BPD-DS) or sleeve gastrectomy (SG) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 months)												
1[q]	randomised trials	very serious[v]	not serious	not serious	serious[p]	none	1/1 study found a positive effect of biliopancreatic diversion with duodenal switch (BPD-DS) or sleeve gastrectomy (SG) plus adjunct therapy intervention on weight loss/maintenance. Mean weight change at 12 months was 42.3kg in the intervention arm versus 38.4kg in the comparator arm.				⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity
Laparoscopic Roux-en-**Y gastric bypass (LRYGB) or sleeve gastrectomy (SG) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 months)**												
2[w]	randomised trials	serious[ab]	serious[ac]	not serious	serious[p]	none	63	115	-	Hedges' g **0.16 lower** (0.98 lower to 0.66 higher)	⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity

Laparoscopic Roux-en-**Y gastric bypass (LRYGB) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 m**onths)												
1[q]	randomised trials	serious[x]	not serious	not serious	serious[p]	none	1/1 study found a negative effect of Laparoscopic Roux-en-Y gastric bypass (LRYGB) plus adjunct therapy compared to bariatric surgery plus usual care/placebo on weight maintenance/loss. BMI decreased by 13.5kg/m^2 in the intervention arm versus 14.5kg/m^2 in the comparator arm.				⊕⊕◯◯ Low	Laparoscopic Roux-en-Y gastric bypass (LRYGB) plus adjunct therapy may result in a large reduction in adiposity.
Roux-en-**Y Gastric Bypass (RYGB) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 months)**												
1[q]	randomised trials	serious[x]	not serious	not serious	serious[p]	none	1/1 study found a small positive effect of Roux-en-Y Gastric Bypass (RYGB) plus adjunct therapy compared to bariatric surgery plus usual care/placebo on weight maintenance/loss. BMI decreased by 16.62kg/m^2 in the intervention arm, versus 16.36kg/m^2 in the comparator group.				⊕⊕◯◯ Low	Roux-en-Y gastric bypass (RYGB) plus adjunct therapy may result in a large reduction in adiposity.
Roux-en-**Y gastric bypass (RYGB) or sleeve gastrectomy (SG) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 months)**												
3[m]	randomised trials	very serious[v]	serious[ad]	not serious	serious[p]	none	172	168	-	Hedges' g **0.14 higher** (0.79 lower to 1.08 higher)	⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity
Roux-en-**Y gastric bypass (RYGB) or sleeve gastrectomy (SG) plus adjunct therapy intervention versus bariatric surgery plus usual care/placebo (baseline to 12 months)**												
1[q]	randomised trials	very serious[v]	not serious	not serious	serious[h]	none	1/1 study found a negative effect for Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) plus adjunct therapy compared to bariatric surgery plus usual care/placebo on weight maintenance/loss Intervention arm lost 30.9% of their body weight versus 31.2% in the comparator arm				⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity

CI: confidence interval

Explanations

a. 16 studies, with 20 intervention arms
b. -1 using RoB-2 risk of bias rated Low (8 (15%) outcomes), Some concerns (36 (68%) outcomes), High (9 (17%) outcomes
c. -2 Inconsistency of I^2=89.87%
d. -1 due to Eggers' g test = 0.00
e. 5 studies, with 5 intervention arms
f. -1 using RoB-2 risk of bias rated Low (2 (13%) outcomes), Some concerns (11 (73%) outcomes), High (2 (13%)
g. -2 inconsistency of I^2=93.00%
h. -1 Imprecision due to small sample size (Total n<400)
i. 11 studies, with 11 intervention arms
j. -1 using RoB-2 risk of bias rated Low (4 (13%) outcomes), Some concerns (21 (70%) outcomes), High (5 (17%) outcomes
k. -2 Inconsistency of I^2=86.29%
l. -1 due to Eggers' g test=0.007
m. 3 studies, with 3 intervention arms
n. -1 using RoB-2 risk of bias rated Low (1 (14%) outcomes), Serious concerns (4 (57%) outcomes), High (2 (29%) outcomes)
o. -2 Inconsistency of I^2=93.40%
p. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)
q. 1 study, with 1 intervention arm
r. -2 Imprecision due to very small size (Total n<50)
s. 8 studies, with 8 intervention arms
t. -2 using RoB-2 risk of bias rated Some concerns (8 (38%) outcomes), High (13 (62%) outcomes)
u. -2 inconsistency of I^2=87.13%
v. -2 using RoB-2 risk of bias rated High for all outcomes
w. 2 studies, with 2 intervention arms
x. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
y. 9 studies, with 9 intervention arms

z. -1 using RoB-2 risk of bias rated Low (1 (5%) outcomes), Some concerns (10 (53%) outcomes), High (8 (42%) outcomes)
aa. -1 Imprecision due to 95% CI crosses 1
ab. -1 using RoB-2 risk of bias rated Low (1 (50%) outcome), Some concerns (1 (50%) outcome)
ac. -1 inconsistency of I^2=73.82%
ad. -1 inconsistency of I^2=74.36%

Older adults (≥65y)

QUESTION

Should nutrition interventions vs. treated/untreated comparators be used for weight maintenance/loss in older adults experiencing overweight or obesity?	
POPULATION:	Older adults living with overweight or obesity
INTERVENTION:	Nutrition interventions: • Nutrition intervention vs any comparator (baseline to 12 months) • Dietary approaches with no specific daily energy intake goal vs any comparator (baseline to 12 months) • Nutrition intervention with a daily energy intake goal vs any comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in older adults. <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (1). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (2). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (3). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (3). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (4, 5). <u>Musculoskeletal conditions</u> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (6, 7). Older adults with obesity undergoing total knee	

	arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (8, 9). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (10). <u>Cancer</u> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (11).	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Nutrition intervention overall ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 2 studies (12, 13) with 4988 intervention participants and 2447 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.61 lower (95%CI 3.37 lower to 2.16 higher) in the intervention versus comparator in nutrition interventions.	
Dietary approaches with no specific daily energy intake goal ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analyses:</u> No evidence was found in this population.	
Nutrition interventions with a daily energy intake goal ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from narrative synthesis:</u> 1 study (13) unable to be included in a meta-analysis found a positive effect of a nutrition intervention with a daily energy target on weight maintenance/loss. The intervention arm reduced body weight by 9.7kg compared to 0.1kg in the comparator arm <u>Additional desirable effects:</u> One review paper found a reduction in total cholesterol for older adults participating in dietary approaches with no specific daily energy intake goal (14). <u>Lived experience:</u> No nutrition-specific reviews were found for the older adult population. The following evidence was taken from studies in the young and middle-aged adult population. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental	

	health, physical function, and reduced body pain (15-18). Reduction in mental health symptoms including depression and anxiety (19, 20), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (21-25). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (26-30). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (30-33). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (34-37). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (34, 35). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (38-41). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (40, 41).	
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Nutrition intervention overall ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Dietary approaches with no specific daily energy intake goal** ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Nutrition interventions with a daily energy intake goal** ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analyses:</u> From 1 study (12) with 4962 intervention participants and 2420 comparator participants, evidence demonstrated a trivial effect size Hedges' g 0.01 higher (95%CI 0.03 lower to 0.06 higher) in the intervention versus comparator in the dietary approaches with no specific daily energy intake goal. <u>Additional undesirable effects:</u>	In adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (48). When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates dietary change, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating.

	No evidence was found in this population. <u>Lived experience:</u> No nutrition-specific reviews available in the older adult population. The following evidence was taken from young and middle-aged adult population. Young and middle-aged adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (28, 34, 39). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (34, 35). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (41). Fears of embarrassment and failure during exercise activities were also reported (32, 39, 41, 42). Cultural and social expectations related to food and alcohol impacted adherence (28, 32) (43). Limited access to culturally appropriate and healthy foods (32), financial constraints (44), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (31, 40, 45-47).	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Nutrition intervention overall ● Very low ○ Low ○ Moderate ○ High ○ No included studies **Dietary approaches with no specific daily energy intake goal** ● Very low ○ Low ○ Moderate ○ High ○ No included studies **Nutrition interventions with a daily energy intake goal** ○ Very low ○ Low ○ Moderate ● High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from meta-analyses:</u> The evidence is very uncertain about the effect of overall nutrition interventions on adiposity. <u>Evidence from meta-analyses:</u> The evidence is very uncertain about the effect of dietary approaches with no specific daily energy intake goal on adiposity. <u>Evidence from narrative synthesis:</u> A nutrition intervention with a daily energy target results in a slight reduction in adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving nutrition treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Nutrition intervention overall ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know **Dietary approaches with no specific daily energy intake goal** ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects favours nutrition intervention overall. Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours dietary approaches with no specific daily energy intake goal.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training. When considering nutrition interventions in older adults living with overweight or obesity, clinicians will need to balance the potential benefit from improving diet quality (and hence improved food and nutrient intakes) versus the need for weight reduction. Healthy dietary approaches with no specific daily energy intake goal may therefore be chosen instead of an intervention with a daily energy goal for the above reasons to balance quality of life. Clinical judgement is required for older adults living with overweight or obesity to balance priorities

Nutrition intervention with a daily energy intake goal ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects favours nutrition interventions with a daily energy goal.	for health care in the presence of co-morbidities (e.g. chronic kidney disease, insulin-requiring Type 2 diabetes mellitus, cancer) as well as age-related conditions (e.g. sarcopenia, osteoporosis/ osteopenia) and treatment with medications that have weight or nutrition requirement implications.
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Nutrition interventions are not necessarily widely available and affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ No included studies	From a payer's perspective, a dietary intervention was cost effective for adults with overweight or obesity and knee osteoarthritis (49). The findings of a randomised controlled trial were that the diet intervention was the most cost-effective approach to reducing weight ($35 per percentage point of weight lost; 2000 US dollars). At 18 months, the diet intervention had superior cost-effectiveness to exercise ($48 per percentage point of weight lost) and exercise and diet ($60 per percentage point of weight lost).	

Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Access to healthy food is still inaccessible or unaffordable for disadvantaged or remote populations. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising the patient's awareness of available treatments and

		avenues for access. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving nutrition treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people living with overweight or obesity, and clinicians.	Acceptability increases where nutrition is individually tailored, and culturally/linguistically appropriate. Accessibility of nutritious, affordable food increases acceptability. The mental health of people should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of nutrition interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	**Moderate**	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	**High**			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Nutrition interventions with a daily energy intake goal and/or dietary approaches with no specific daily energy intake goal:
<u>Consensus statement due to limited evidence:</u>

Nutrition interventions with a daily energy intake goal and/or dietary approaches with no specific daily energy intake goal may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

Dietary approaches with no specific daily energy intake goal:
<u>Consensus statement due to limited evidence:</u>
Dietary approaches with no specific daily energy intake goal may be encouraged as part of a comprehensive approach for management of weight-related health and wellbeing.

Nutrition interventions with a daily energy intake goal:
<u>Consensus statement due to limited evidence:</u>
Nutrition interventions with a daily energy intake goal may be encouraged, for individuals for whom weight loss is the primary goal, as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
2. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
3. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
4. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
5. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
6. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
7. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
8. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
9. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
10. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
11. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
12. Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Fitó M, Chiva-Blanch G, et al. Effect of a high-fat Mediterranean diet on bodyweight and waist circumference: a prespecified secondary outcomes analysis of the PREDIMED randomised controlled trial. Lancet Diabetes Endocrinol. 2019;7(5):e6-e17. doi: 10.1016/S2213-8587(19)30074-9
13. Villareal DT, Chode S, Parimi N, Sinacore DR, Hilton T, Armamento-Villareal R, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med. 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234
14. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. Age Ageing. 2010;39(2):176-84. doi: 10.1093/ageing/afp251
15. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
16. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317

17. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
18. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
19. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
20. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
21. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
22. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
23. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
24. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
25. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
26. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
27. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
28. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
29. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
30. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
31. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
32. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
33. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
34. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
35. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
36. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
37. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815

38. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
39. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
40. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
41. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
42. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
43. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
44. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
45. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
46. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
47. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227
48. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
49. Sevick MA, Miller GD, Loeser RF, Williamson JD, Messier SP. Cost-effectiveness of exercise and diet in overweight and obese adults with knee osteoarthritis. Med Sci Sports Exerc. 2009;41(6):1167-74. doi: 10.1249/MSS.0b013e318197ece7

Question: Nutrition interventions compared to treated/untreated comparators for weight maintenance/loss in older adults experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	nutrition interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Nutrition interventions with a daily energy intake goal and/or dietary approaches with no specific daily energy intake goal vs any comparator (baseline to 12 months) - meta-analysis												
2[a]	randomised trials	very serious[b]	very serious[c]	not serious	serious[d]	none	4988	2447	-	Hedges' g **0.61 lower** (3.37 lower to 2.16 higher)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity
Nutrition intervention with no **specific daily energy intake goal vs any comparator (baseline to 12 months)** - meta-analysis												
1[e]	randomised trials	very serious[f]	not serious	not serious	serious[d]	none	4962	2420	-	Hedges' g **0.01 higher** (0.03 lower to 0.06 higher)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity
Nutrition intervention with a daily energy **target vs any comparator (baseline to 12 months)** - narrative synthesis												
1[g]	randomised trials	serious[h]	not serious	not serious	serious[i]	very strong association	1/1 study found a positive effect of nutrition intervention with a daily energy target on weight maintenance/loss. The intervention arm reduced body weight by 9.7kg compared to 0.1kg in the comparator arm				⨁⨁⨁⨁ High	A nutrition intervention with a daily energy target results in a slight reduction in adiposity

CI: confidence interval

Explanations

a. 2 studies, with 3 intervention arms
b. -2 using RoB-2 risk of bias was rated Some concerns (2 (33%) outcomes), High (4 (67%) outcomes)
c. -2 Inconsistency of I^2=99.81%
d. -1 Imprecision due to 95% CI crosses 1
e. 1 study, with 2 intervention arms
f. -2 using RoB-2 risk of bias all outcomes rated High
g. 1 study, with 1 intervention arm
h. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
i. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should physical activity interventions vs. treated/untreated comparators be used for weight maintenance/loss in older adults experiencing overweight or obesity?	
POPULATION:	Older adults living with overweight or obesity
INTERVENTION:	Physical activity interventions: • Physical activity intervention vs untreated comparator (baseline to 12 months) • Strengthening exercise intervention vs untreated comparator (baseline to 12 months) • Combination of aerobic exercise and strengthening exercise interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in older adults. <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (1). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (2). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (3). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (3). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (4, 5). <u>Musculoskeletal conditions</u> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (6, 7). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (8, 9). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis	

	experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (10). <u>Cancer</u> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (11).	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Physical activity intervention overall ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know **Strengthening exercise intervention** ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know **Aerobic exercise and strengthening exercise intervention** ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 3 studies (12-14) with 123 intervention participants and 123 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.65 lower (2.25 lower to 0.95 higher) in the physical activity intervention versus comparator. <u>Evidence from narrative synthesis:</u> 1 study (15) unable to be included in a meta-analysis found a positive effect of strengthening exercise on weight maintenance/loss. BMI decreased in the intervention arm by $2.8kg/m^2$ and by $0.5kg/m^2$ in the comparator arm. <u>Evidence from meta-analyses:</u> From 2 studies (13, 14) with 61 intervention participants and 58 comparator participants, evidence demonstrated a small important effect of Hedges' g 0.27 lower (0.61 lower to 0.08 higher) in the intervention combining aerobic exercise and strengthening exercise versus comparator. <u>Additional desirable effects:</u> No evidence was found in this population. <u>Lived experience:</u> No reviews were identified in the older adult population. The following evidence was taken from studies of young and middle-aged adults. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (16-19). Reduction in mental health symptoms including depression and anxiety (20, 21), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (22-26). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (27-31). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (31-34). Strategies such as group interventions, goal setting, food/activity logs,	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (43), Healthy China Initiative (44), Finnish Diabetes Prevention Study (45)) overwhelmingly support positive health outcomes of physical activity. In young to middle-aged adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (46).

	and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (35-38). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (35, 36). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (39-42). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (41, 42).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Physical activity intervention overall ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Strengthening exercise intervention** ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know **Aerobic exercise and strengthening exercise intervention** ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analyses:</u> No evidence was found in this population. <u>Additional undesirable effects:</u> No evidence was found in this population. <u>Lived experience:</u> No reviews were identified in the older adult population. The following evidence was taken from studies of young and middle-aged adults. Young and middle-aged adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (29, 35, 40). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (35, 36). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (42). Fears of embarrassment and failure during exercise activities were also reported (33, 40, 42, 47). Cultural and social expectations related to food and alcohol impacted adherence (29, 33) (48). Limited access to culturally appropriate and healthy foods (33), financial constraints (49), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (32, 41, 50-52).	A low risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Physical activity intervention overall ● Very low ○ Low ○ Moderate ○ High	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from meta-analyses:</u> The evidence is very uncertain about the effect of physical activity interventions on adiposity.	

○ No included studies **Strengthening exercise intervention overall** ○ Very low ○ Low ● Moderate ○ High ○ No included studies **Aerobic exercise and strengthening exercise intervention** ○ Very low ● Low ○ Moderate ○ High ○ No included studies	<u>Evidence from narrative synthesis:</u> Strengthening exercise likely reduces adiposity slightly. <u>Evidence from meta-analyses:</u> Combining aerobic exercise and strengthening exercise may reduce adiposity slightly.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of older adults living with overweight or obesity in relation to receiving physical activity treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Physical activity intervention overall ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training. Clinical judgement is required for older adults living with overweight or

Strengthening exercise intervention overall o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favours the intervention o Varies o Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	obesity to balance priorities for health care in the presence of co-morbidities (e.g. chronic kidney disease, insulin-requiring Type 2 diabetes mellitus, cancer) as well as age-related conditions (e.g. sarcopenia, osteoporosis/ osteopenia) and treatment with medications that have weight or nutrition requirement implications.
Aerobic exercise and strengthening exercise intervention o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favours the intervention o Varies o Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Physical activity interventions are not necessarily widely available and affordable.	Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the

		intervention to be provided, and who provides it.

Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
o Very low o Low o Moderate o High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours the intervention o Favours the intervention o Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased ● Varies o Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some older people, decreasing health equity. Access to facilities, tailoring of exercise programs specifically for older adults and mobility issues also need to be considered. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical

		activity programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where physical activity is individually tailored and appropriate. Acceptable where mental health of the participant is considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of physical activity interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	**Low**	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation
Aerobic and/or strengthening exercise interventions: Consensus statement due to limited evidence: Aerobic and/or strengthening exercise interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing. Strengthening exercise interventions: Consensus statement due to limited evidence: Strengthening exercise interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing. Combined aerobic and strengthening exercise interventions: Conditional recommendation for the intervention: Aerobic and strengthening exercise interventions may be recommended as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
2. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
3. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
4. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
5. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
6. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
7. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
8. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
9. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
10. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
11. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
12. Gallè F, Di Onofrio V, Romano Spica V, Mastronuzzi R, Russo Krauss P, Belfiore P, et al. Improving physical fitness and health status perception in community-dwelling older adults through a structured program for physical activity promotion in the city of Naples, Italy: a randomized controlled trial. Geriatr Gerontol Int. 2017;17(10):1421-8. doi: 10.1111/ggi.12879
13. Hojan K, Kwiatkowska-Borowczyk E, Leporowska E, Milecki P. Inflammation, cardiometabolic markers, and functional changes in men with prostate cancer. A randomized controlled trial of a 12-month exercise program. Pol Arch Intern Med. 2017;127(1):25-35. doi: 10.20452/pamw.3888
14. Villareal DT, Chode S, Parimi N, Sinacore DR, Hilton T, Armamento-Villareal R, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med. 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234

15. Winters-Stone KM, Dieckmann N, Maddalozzo GF, Bennett JA, Ryan CW, Beer TM. Resistance exercise reduces body fat and insulin during androgen-deprivation therapy for prostate cancer. Oncol Nurs Forum. 2015;42(4):348-56. doi: 10.1188/15.ONF.348-356
16. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
17. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
18. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
19. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
20. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
21. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
22. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
23. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
24. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
25. Palavras MA, Hay P, Filho CADS, Claudino A. The fficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
26. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
27. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
28. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
29. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
30. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
31. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
32. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
33. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
34. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
35. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583

36. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
37. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
38. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
39. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
40. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
41. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
42. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
43. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
44. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
45. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
46. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
47. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
48. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
49. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
50. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
51. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
52. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Physical activity interventions compared to treated/untreated comparators for weight maintenance/loss in older adults experiencing overweight/obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	Other **considerations**	**physical activity** interventions	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Physical activity intervention vs untreated comparator (baseline to 12 months)												
3[a]	randomised trials	serious[b]	very serious[c]	not serious	serious[d]	none	123	123	-	Hedges' g 0.65 **lower** (2.25 lower to 0.95 higher)	⊕◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity
Combination of aerobic exercise and strengthening exercise interventions vs untreated comparator (baseline to 12 months)												
2[e]	randomised trials	serious[f]	not serious	not serious	serious[d]	none	61	58	-	Hedges' g **0.27 lower** (0.61 lower to 0.08 higher)	⊕⊕◯◯ Low	Combining aerobic exercise and strengthening exercise may reduce adiposity slightly
Strengthening exercise intervention vs untreated comparator (baseline to 12 months)												
1[g]	randomised trials	very serious[h]	not serious	not serious	serious[i]	very strong association	1/1 study found a positive effect of strengthening exercise on weight maintenance/loss. BMI decreased in the intervention arm by 2.8kg/m^2 and by 0.5kg/m^2 in the comparator arm.				⊕⊕⊕◯ Moderate	Strengthening exercise likely reduces adiposity slightly

CI: confidence interval

Explanations

a. 3 studies, with 3 intervention arms
b. -1 using RoB-2 risk of bias rated Some concerns (4 (80%) outcomes), High (1 (20%) outcomes)
c. -2 Inconsistency of I^2=87.56%
d. -1 Imprecision due to 95% CI crosses and small sample size (Total n<400)
e. 2 studies, with 2 intervention arms
f. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
g. 1 study, with 1 intervention arm
h. -2 using RoB-2 risk of bias rated High for all outcomes
i. -1 level due to small sample size (total n<400)

QUESTION

Should interventions combining nutrition and physical activity with or without sedentary behaviour vs. treated/untreated comparators be used for weight maintenance/loss in older adults experiencing overweight or obesity?	
POPULATION:	Older adults living with overweight or obesity
INTERVENTION:	Combined nutrition and physical activity interventions with or without sedentary behaviour interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in older adults. <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (1). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (2). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (3). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (3). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (4, 5). <u>Musculoskeletal conditions</u> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (6, 7). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (8, 9). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (10).	

	<u>Cancer</u> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (11).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 4 studies (12-15) with 570 intervention participants and 570 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.65 lower (2.12 lower to 0.82 higher) in the nutrition and physical activity interventions with or without sedentary behaviour interventions versus an untreated comparator. <u>Additional desirable effects:</u> Additional desirable effects experienced by older adults participating in nutrition and physical activity interventions included reduced total cholesterol (16). <u>Lived experience:</u> No reviews were identified in the older adult population. The following evidence was taken from studies of young and middle-aged adults. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (17-20). Reduction in mental health symptoms including depression and anxiety (21, 22), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (23-27). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (28-32). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (32-35). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (36-39). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (36, 37). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (40-43). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (42, 43).	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (44), Healthy China Initiative (45), Finnish Diabetes Prevention Study (46)) overwhelmingly support positive health outcomes of physical activity. In young to middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (47). Similarly, taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (47).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate	<u>Evidence from meta-analyses:</u> No evidence was found in this population. <u>Additional undesirable effects:</u>	When older people who are living with overweight or obesity are participating in a behavioural weight loss

○ Large ○ Varies ● Don't know	No evidence was found in this population. <u>Lived experience:</u> No reviews were identified in the older adult population. The following evidence was taken from young and middle-aged adult population. Young and middle-aged adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (30, 36, 41). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (36, 37). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (43). Fears of embarrassment and failure during exercise activities were also reported (34, 41, 43, 48). Cultural and social expectations related to food and alcohol impacted adherence (30, 34) (49). Limited access to culturally appropriate and healthy foods (34), financial constraints (50), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (33, 42, 51-53).	intervention that incorporates dietary change, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. A low but real risk of incidental musculoskeletal injury exists for older people with overweight or obesity during physical activity. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. The evidence is very uncertain about the effect of nutrition and physical activity interventions on adiposity. The evidence is very uncertain about the effect of nutrition and physical activity and sedentary behaviour interventions on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving combined nutrition and physical activity treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favours the intervention o Varies o Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training. When considering nutrition interventions in older adults living with overweight or obesity, clinicians will need to balance the potential benefit from improving diet quality (and hence improved food and nutrient intakes) versus the need for weight reduction. Healthy dietary approaches with no specific daily energy intake goal may therefore be chosen instead of an energy target diet for the above reasons to balance quality of life. Clinical judgement is required for older adults living with overweight or obesity to balance priorities for health care in the presence of co-morbidities (e.g. chronic kidney disease, insulin-requiring Type 2 diabetes mellitus, cancer) as well as age-related conditions (e.g. sarcopenia, osteoporosis/osteopenia, etc.) and treatment with medications that have weight or nutrition requirement implications.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition and physical activity interventions are not necessarily widely available and affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours the intervention o Favours the intervention o Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some older people, decreasing health equity. Access to facilities, tailoring of exercise programs specifically for older adults and mobility issues also need to be considered. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight

		management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition and physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people living with overweight or obesity, and clinicians.	Acceptability increases where nutrition and physical activity are individually tailored and culturally appropriate. Acceptable where mental health of the participant is considered and monitored.

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of nutrition and physical activity interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:
Combined nutrition and physical activity interventions are encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
2. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
3. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
4. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
5. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
6. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
7. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
8. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
9. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
10. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
11. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
12. Demark-Wahnefried W, Morey MC, Sloane R, Snyder DC, Miller PE, Hartman TJ, Cohen HJ. Reach out to enhance wellness home-based diet-exercise intervention promotes reproducible and sustainable long-term improvements in health behaviors, body weight, and physical functioning in older, overweight/obese cancer survivors. J Clin Oncol. 2012;30(19):2354-61. doi: 10.1200/JCO.2011.40.0895
13. Herrera-Espiñeira C, Martínez-Cirre MdC, López-Morales M, Lozano-Sánchez A, Rodríguez-Ruíz A, Salmerón-López LE, et al. Hospital intervention to reduce overweight with educational reinforcement after discharge: a multicenter randomized clinical trial. Nutrients. 2022;14(12):2499. doi: 10.3390/nu14122499
14. Serra-Prat M, Terradellas M, Lorenzo I, Arús M, Burdoy E, Salietti A, et al. Effectiveness of a weight-loss intervention in preventing frailty and functional decline in community-dwelling obese older people. A randomized controlled trial. J Frailty Aging. 2022;11(1):91-9. doi: 10.14283/jfa.2021.38
15. Villareal DT, Chode S, Parimi N, Sinacore DR, Hilton T, Armamento-Villareal R, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med. 2011;364(13):1218-29. doi: 10.1056/NEJMoa1008234
16. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. Age Ageing. 2010;39(2):176-84. doi: 10.1093/ageing/afp251
17. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
18. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317

19. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
20. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
21. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
22. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
23. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
24. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
25. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
26. Palavras MA, Hay P, Filho CADS, Claudino A. The ffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
27. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
28. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
29. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
30. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
31. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
32. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
33. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
34. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
35. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
36. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
37. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
38. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
39. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
40. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017

41. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
42. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
43. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
44. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
45. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
46. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
47. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
48. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
49. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
50. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
51. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
52. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
53. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition and physical activity with or without sedentary behaviour compared to treated/untreated comparators for weight maintenance/loss in older adults experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	interventions combining nutrition and physical activity with or without sedentary behaviour	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Nutrition and physical activity with or without sedentary behaviour interventions vs untreated comparator (baseline to 12 months) – Meta-**analysis**												
4[a]	randomised trials	very serious[b]	not serious	very serious[c]	serious[d]	strong association	570	570	-	Hedges' g **0.65 lower** (2.12 lower to 0.82 higher)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity

CI: confidence interval

Explanations

a. 4 studies, with 4 intervention arms
b. -2 using RoB-2 risk of bias rated Some concerns (3 (27%) outcomes), High (8 (73%) outcomes)
c. -2 Inconsistency of I^2=97.91%
d. -1 Imprecision due to 95% CI crosses 1

QUESTION

Should interventions combining nutrition, physical activity and psychological vs. treated/untreated comparators be used for weight maintenance/loss in older adults experiencing overweight or obesity?	
POPULATION:	Older adults living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and psychological interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
o No o Probably no o Probably yes ● Yes o Varies o Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in older adults. <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (1). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (2). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (3). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (3). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (4, 5). <u>Musculoskeletal conditions</u> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (6, 7). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (8, 9). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (10). <u>Cancer</u>	

	A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (11).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Evidence from meta-analyses: From 2 studies (12, 13) with 98 intervention participants and 100 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.22 lower (95%CI 0.49 lower to 0.06 higher) in nutrition, physical activity, and psychological interventions versus untreated comparator. Evidence from narrative synthesis: 1 additional study (14) unable to be included in the meta-analysis found a positive effect of combining nutrition, physical activity, and psychological interventions on weight maintenance/loss. Weight reduced by 2.9kgs in the intervention arm compared to a reduction of 0.2kgs in the comparator arm. Additional desirable effects: No evidence was identified in this population. Lived experience: No evidence was identified in this population. The following evidence was taken from studies of young and middle-aged adults. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (15-18). Reduction in mental health symptoms including depression and anxiety (19, 20), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (21-25). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (26-30). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (30-33). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (34-37). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (34, 35). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (38-41). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (40, 41).	Current available data indicates a reduction in eating disorder symptoms (binge eating disorder) with weight loss treatments. Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (42), Healthy China Initiative (43), Finnish Diabetes Prevention Study (44)) overwhelmingly support positive health outcomes of physical activity. In young to middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (45). Similarly, taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (45).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Trivial o Small o Moderate o Large o Varies ● Don't know	<u>Evidence from meta-analyses:</u> No evidence was found in this population. <u>Additional undesirable effects:</u> No evidence was found in this population. <u>Lived experience</u>: No evidence was identified in this population. The following evidence was taken from studies of young and middle-aged adults. Young and middle-aged adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (28, 34, 39). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (34, 35). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (41). Fears of embarrassment and failure during exercise activities were also reported (32, 39, 41, 46). Cultural and social expectations related to food and alcohol impacted adherence (28, 32) (47). Limited access to culturally appropriate and healthy foods (32), financial constraints (48), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (31, 40, 49-51).	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates dietary change, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. A low risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, including realistic goals, should be developed for older people experiencing overweight or obesity. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ● Low o Moderate o High o No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. <u>Evidence from meta-analysis:</u> Nutrition, physical activity, and psychological interventions may reduce adiposity slightly. <u>Evidence from narrative synthesis:</u> The evidence is very uncertain about the effect of nutrition, physical activity, and psychological interventions on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Important uncertainty or	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving	Some people living with overweight or obesity

variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	combined nutrition, physical activity, and psychological treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	(possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training. When considering nutrition interventions in older adults living with overweight or obesity, clinicians will need to balance the potential benefit from improving diet quality (and hence improved food and nutrient intakes) versus the need for weight reduction. Healthy dietary approaches with no specific daily energy intake goal may therefore be chosen instead of an energy target diet for the above reasons to balance quality of life. Clinical judgement is required for older adults living with overweight or obesity to balance priorities for health care in the presence of co-morbidities (e.g. chronic kidney disease, insulin-requiring Type 2 diabetes mellitus, cancer) as well as age-related conditions (e.g. sarcopenia, osteoporosis/ osteopenia) and treatment with

		medications that have weight or nutrition requirement implications.
Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition, physical activity and psychological interventions are not necessarily widely available and affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Participants reported financial barriers to structured physical activity, included expensive gym memberships, equipment, and clothing. Long-term psychological care is often needed, and treatment is unlikely to be one-off. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the	From a payer's perspective, a 12-month digital Type 2 diabetes mellitus prevention program focusing on behaviour change had no significant effect on medical costs at 12 and 24 months (52).	

intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies		

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some older people, decreasing health equity. Access to facilities, tailoring of exercise programs specifically for older adults and mobility issues also need to be considered. High cost of psychological care and long wait times may make treatment prohibitive for some older people, decreasing health equity. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be

		culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising the patient’s awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs, or when discussing the patient’s care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition, physical activity, and psychological treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people living with overweight or obesity, and clinicians.	Acceptability increases where nutrition, physical activity and psychological treatments are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. The mental health of people should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition, physical activity and psychological interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	**Does not favour either the intervention or the comparison**	Probably favours the intervention	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation
Conditional recommendation for the intervention: Combined nutrition, physical activity and psychological interventions may be recommended as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
2. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
3. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
4. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
5. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
6. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
7. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
8. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
9. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
10. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
11. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
12. Gillison F, Stathi A, Reddy P, Perry R, Taylor G, Bennett P, et al. Processes of behavior change and weight loss in a theory-based weight loss intervention program: a test of the process model for lifestyle behavior change. Int J Behav Nutr Phys Act. 2015;12:2. doi: 10.1186/s12966-014-0160-6
13. Greaves C, Gillison F, Stathi A, Bennett P, Reddy P, Dunbar J, et al. Waste the waist: a pilot randomised controlled trial of a primary care based intervention to support lifestyle change in people with high cardiovascular risk. Int J Behav Nutr Phys Act. 2015;12:1. doi: 10.1186/s12966-014-0159-z
14. Rumbo-Rodríguez L, Zaragoza-Marti A, Sánchez-SanSegundo M, Ferrer-Cascales R, Laguna-Pérez A, Hurtado-Sánchez JA. Effectiveness of a two-year multicomponent intervention for the treatment of overweight and obesity in older people. Nutrients. 2022;14(22):4762. doi: 10.3390/nu14224762
15. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
16. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
17. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261

18. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
19. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
20. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
21. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
22. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
23. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
24. Palavras MA, Hay P, Filho CADS, Claudino A. The fflicacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
25. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
26. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
27. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
28. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
29. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
30. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
31. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
32. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
33. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
34. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
35. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
36. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
37. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
38. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
39. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350

40. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
41. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
42. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
43. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
44. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
45. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
46. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
47. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
48. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
49. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
50. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
51. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227
52. Smith DH, O'Keeffe-Rosetti M, Fitzpatrick SL, Mayhew M, Firemark AJ, Gruss I, et al. Costs and Cost-Effectiveness of Implementing a Digital Diabetes Prevention Program in a Large, Integrated Health System. Perm J. 2022;26(3):74-82. doi: 10.7812/TPP/22.029

Question: Interventions combining nutrition, physical activity and psychological compared to treated/untreated comparators for weight maintenance/loss in older adults experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	interventions **combining nutrition, physical activity and psychological**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Nutrition, physical activity, and psychological interventions vs untreated comparator (baseline to 12 months) - **meta-analysis**												
2[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	none	98	100	-	Hedges' g **0.22 lower** (0.49 lower to 0.06 higher)	⨁⨁◯◯ Low	Nutrition, physical activity, and psychological interventions may reduce adiposity slightly
Nutrition, physical activity, and psychological interventions vs untreated comparator (baseline to 12 months) - narrative synthesis												
1[d]	randomised trials	very serious[e]	not serious	not serious	very serious[f]	none	1/1 study found a positive effect of combining nutrition, physical activity, and psychological interventions on weight maintenance/loss Weight reduced by 2.9kgs in the intervention arm compared to a reduction of 0.2kgs in the comparator arm				⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 2 studies, with 2 intervention arms
b. -1 using RoB-2 risk of bias rated Low (1 (50%) outcomes), Some concerns (1 (50%) outcomes)
c. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)
d. 1 study, with 1 intervention arm
e. -2 using RoB-2 risk of bias rated High for all outcomes
f. -2 Imprecision due to very small size (Total n<50)

QUESTION

Should interventions combining nutrition and sedentary behaviour interventions vs. treated/untreated comparators be used for weight maintenance/loss in older adults experiencing overweight or obesity?	
POPULATION:	Older adults living with overweight or obesity
INTERVENTION:	Combined nutrition and sedentary behaviour interventions vs any comparator (baseline to final end-point)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Our review of the evidence demonstrated a number of health risks associated with overweight and obesity in older adults. <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (1). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (2). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (3). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (3). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (4, 5). <u>Musculoskeletal conditions</u> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (6, 7). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (8, 9). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (10).	

<table>
<tr><td></td><td><u>Cancer</u>
A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (11).</td><td></td></tr>
<tr><td colspan="3">Desirable Effects
How substantial are the desirable anticipated effects?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>○ Trivial
● Small
○ Moderate
○ Large
○ Varies
○ Don't know</td><td><u>Evidence from narrative synthesis:</u>
1 study (12) unable to be included in a meta-analysis favoured combining nutrition and sedentary behaviour interventions for weight maintenance/loss. Body weight reduced by 6.4 kgs in the intervention arm vs 4.4 kgs in the comparator arm after 18 months.

<u>Additional desirable effects:</u>
No evidence was found in this population.

<u>Lived Experience:</u>
No evidence was identified in this population. The following evidence was taken from studies of young and middle-aged adults.

Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (13-16). Reduction in mental health symptoms including depression and anxiety (17, 18), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (19-23). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (24-28). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (28-31). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (32-35).

Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (32, 33). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (36-39). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (38, 39).</td><td></td></tr>
<tr><td colspan="3">Undesirable Effects
How substantial are the undesirable anticipated effects?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>○ Trivial
● Small
○ Moderate
○ Large
○ Varies
○ Don't know</td><td><u>Evidence from meta-analyses:</u>
No evidence was found in this population.

<u>Additional undesirable effects:</u>
No evidence was found in this population.

<u>Lived experience:</u>
No evidence was identified for the older adult population. The</td><td>In addition to intentional adiposity loss, some older people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) and may be at increased risk of developing sarcopenia whilst</td></tr>
</table>

	following evidence was taken from studies of young and middle-aged adults. Young and middle-aged adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (26, 32, 37). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (32, 33). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (39). Fears of embarrassment and failure during exercise activities were also reported (30, 37, 39, 40). Cultural and social expectations related to food and alcohol impacted adherence (26, 30) (41). Limited access to culturally appropriate and healthy foods (30), financial constraints (42), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (29, 38, 43-45).	undergoing weight-loss treatment. When older people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates dietary change, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Nutrition and sedentary behaviour interventions may decrease adiposity slightly.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving combined nutrition and sedentary behaviour treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training. When considering nutrition interventions in older adults living with overweight or obesity, clinicians will need to balance the potential benefit from improving diet quality (and hence improved food and nutrient intakes) versus the need for weight reduction. Healthy dietary approaches with no specific daily energy intake goal may therefore be chosen instead of an energy target diet for the above reasons to balance quality of life. Clinical judgement is required for older adults living with overweight or obesity to balance priorities for health care in the presence of co-morbidities (e.g. chronic kidney disease, insulin-requiring Type 2 diabetes mellitus, cancer) as well as age-related conditions (e.g. sarcopenia, osteoporosis/ osteopenia) and treatment with medications that have weight or nutrition requirement implications.

Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ○ Moderate costs ○ Negligible costs and	We have not sourced literature on the resources required for this intervention.	Dietitians are expensive for patients via the private system, and there is a lack of

savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	Combined nutrition and sedentary behaviour interventions are not necessarily widely available and affordable.	availability through public health system. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.
Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	
Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of combined nutrition and sedentary behaviour interventions was identified in older adults.	
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. Social and health factors are interconnected and

		complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving combined nutrition and sedentary behaviour treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Acceptability increases where nutrition and sedentary behaviour interventions are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. The mental health of older people should be considered and monitored.

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of combined nutrition and sedentary behaviour interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Clinical judgement is required for older adults living with overweight or obesity to balance priorities for health care in the presence of co-morbidities (e.g. chronic kidney disease, insulin-requiring Type 2 diabetes mellitus, cancer) as well as age-related conditions (e.g. sarcopenia, osteoporosis/osteopenia, etc.) and treatment with medications that have weight or nutrition requirement implications.

Consensus statement due to limited evidence:
Combined nutrition and sedentary behaviour interventions are encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
2. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
3. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
4. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
5. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
6. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
7. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
8. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
9. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
10. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
11. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
12. Flores-Mateo G, Rojas-Rueda D, Basora J, Ros E, Salas-Salvadó J. Nut intake and adiposity: meta-analysis of clinical trials. Am J Clin Nutr. 2013;97(6):1346-55. doi: 10.3945/ajcn.111.031484
13. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
14. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
15. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
16. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556

17. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
18. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
19. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
20. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
21. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
22. Palavras MA, Hay P, Filho CADS, Claudino A. The fficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
23. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
24. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
25. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
26. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
27. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
28. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
29. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
30. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
31. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
32. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
33. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
34. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
35. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
36. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
37. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
38. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473

39. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
40. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
41. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
42. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
43. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
44. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
45. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition and sedentary behaviour compared to treated/untreated comparators for weight maintenance/loss in older adults experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	Inconsistency	Indirectness	Imprecision	Other considerations			
Nutrition and sedentary behaviour interventions vs any comparator (baseline to final end-point)									
1[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	none	1/1 studies favoured combining nutrition and sedentary behaviour interventions for weight maintenance/loss. Body weight reduced by 6.4 kgs in the intervention arm vs 4.4 kgs in the comparator arm after 18 months.	⨁⨁◯◯ Low	Nutrition and sedentary behaviour interventions may decrease adiposity slightly

CI: confidence interval

Explanations

a. 1 study, with 1 intervention arm
b. -1 using RoB-2 risk of bias rated Some concerns for all studies
c. -1 Imprecision due to small sample size (Total n<400)

People living with a disability

QUESTION

Should nutrition interventions vs. treated/untreated comparators be used for weight maintenance/loss in individuals with a disability experiencing overweight or obesity?	
POPULATION:	People with a disability living with overweight or obesity
INTERVENTION:	Nutrition interventions: • Nutrition intervention vs untreated comparator (baseline to 12 months) • Dietary approaches with no specific daily energy intake goal vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Obesity rates are higher among people with disabilities than those without disabilities (1-3). Statistics on people aged ≥2 years living in households in Australia show that the prevalence of overweight and obesity is higher among people with disabilities (72%) than those without disabilities (55%) (2). The disparity between people with and without disabilities in Australia is consistent with international evidence where, for example, the obesity rates of community-dwelling people with disabilities in the US (37%) are much higher than the general population (27%) (3). Obesity can be one aspect of complex health profiles of people with disabilities (4). People with intellectual disability, for example, have high rates of obesity (estimates range from 3.9% to 34.8%) in combination with other physical health conditions, such as epilepsy (9.0% to 51.8%), visual impairment (3.2% to 47.0%), hearing loss (1.4% to 34.9%), osteoporosis (1.7% to 41.0%), cerebral palsy (1.0% to 28.9%), and microcephaly (20.9%) (4). Variations in the ages and intellectual disability severity are likely explanations for the wide ranges in estimates (4). Factors associated with obesity among people with disabilities include poor diet quality (5), low physical activity levels (5), various medications (6), impairment types (6), functional limitations (1), diagnostic overshadowing (7), and environmental barriers (1). Compared with people without disabilities, people with disabilities living in households in Australia had a higher daily consumption of sugar-sweetened beverages (8.3% versus 5.6%) were slightly less likely to be meeting guidelines for fruit and vegetable consumption (45% versus 49%), and more likely to exceed the weekly alcohol consumption guideline (23% versus 19%) (5). Three quarters (74%) of people with disabilities in Australia are not meeting physical activity guidelines, which is similar to those without disability (71%) (5). With respect to medications, many people with intellectual disability, for example, take medications that can cause weight gain, such as second-generation antipsychotics, antidepressants (e.g.,	72% of Australians with a disability (aged 2 and over) are also living with overweight or obesity, compared with 55% of those without disability (2). 75% Australian males with a disability (aged 2 and over) are living with overweight or obesity. 69% of Australian females with a disability (aged 2 and over) are living with overweight or obesity (2). 79% of older Australians (aged 65 and over) with a disability are also living with overweight or obesity. 68% of younger Australians (aged under 65) with a disability are also living with overweight or obesity (2). 54% Australian adults with disability have hypertension, compared with 27% without a disability. 32% with uncontrolled (or high) blood pressure (2).

	Paxil, Zoloft), anticonvulsants (e.g., Depakote), antihypertensives (e.g., Cardura, Inderal), and antidiabetics (e.g., Diabeta, Diabinese) (6). People with certain impairments (e.g., Down syndrome) are more susceptible to weight gain (6). Functional limitations can pose barriers to engaging fully in healthy activities, such as physical activity (1). Diagnostic overshadowing can mean that obesity symptoms are overlooked or attributed to patients' impairments, resulting in substandard care for obesity (7). Numerous environmental barriers (e.g., inaccessible environments, fewer health promotion programs accessible for people with disabilities) serve to limit the potential of people with disabilities to engage in activities to prevent or manage overweight and obesity. **People with a disability** Only one systematic review was identified in people with a disability, specifically cerebral palsy. No other reviews of people with other disabilities were identified. The review of cross-sectional and cohort studies in adults with cerebral palsy showed that having overweight or obesity was the most commonly cited cardiovascular disease risk factor (8). While very limited evidence was identified in people with a disability, our review demonstrated a number of health risks associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y). **Children and adolescents (2 to <18y)** <u>Blood pressure indicators</u> Prevalence of prehypertension (9), hypertension and elevated blood pressure (9-14) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (15). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (16, 17). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (9, 12-14). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (15). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (16, 18) and mortality (17, 18) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (17).	

	<u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (9, 13, 14). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (13, 14). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (16-18). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (13) and risk of developing non-alcoholic fatty liver disease (9, 19-21) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (22). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (23). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (24), and ovarian (24, 25) cancer during adulthood among women; and colorectal cancer (26) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (27). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (13) and depression (13, 28) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (29). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (30). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (13). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic	

	ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (31). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (32). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (32). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (32). **Young and middle-aged adults (18 to <65y)** <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (33-44). Cardiovascular disease mortality increased with increasing weight (43, 45-47). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (48, 49), including ischemic stroke (48), and haemorrhagic stroke (48). Risk was also elevated for coronary artery disease (50, 51). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or ‘other’ causes, compared to healthy weight survivors (52). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (53). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants’ risk of mortality from cardiovascular disease decreased (37, 54-56). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (57). <u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (41, 51, 58-73). Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (37, 57, 74-77). <u>Non-alcoholic fatty liver disease</u> Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (78-83).	

	Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (84-86). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (84). <u>Musculoskeletal conditions</u> Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (87). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (88). <u>Cancer</u> When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (89, 90), thyroid (90-96), and blood cancers such as; lympho-haematopoietic (97) and diffuse large B-cell lymphoma (98, 99), multiple myeloma (90, 99-101), Hodgkin and non-Hodgkin lymphoma (90, 99), and leukemia (102, 103) (obesity only (104)). Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (73, 89, 90, 95, 101, 102, 105-110), gastroesophageal (111, 112), gastric (90, 95, 110, 113, 114), and stomach (73) cancers; and liver (73, 90, 95, 101, 112, 115-124), gallbladder (73, 90, 101, 102, 125-127), bile duct (128), pancreatic (73, 95, 101, 102, 112, 129-131), small intestinal (129), and colorectal (89, 90, 95, 101, 102, 112, 130, 132-149) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (73, 89, 90, 95, 101, 102, 112, 142, 150-154), and bladder (73, 90, 152, 153, 155-158)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (102) cancers, and total cancer risk was associated with increasing adiposity (159). Increased BMI in adulthood (≥18y) was protective against lung cancer (89, 160, 161), and pre-menopausal breast cancer (89, 162). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (163). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (164). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (90, 112, 165-168) (premenopausal (95, 169, 170) or postmenopausal (142) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (171). Risk of other gynaecological cancers also increased, including endometrial (89, 90, 101, 102, 139, 142, 172-175), uterine (73), and cervical cancers (90) (weak association with obesity (176)), as well as breast cancer (95, 102, 112, 139, 142, 159, 176-188). There was a greater risk of total and breast cancer	

	mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (52). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (152, 189, 190), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (89, 191), while risk increased for development of advanced prostate cancer (112, 153, 191, 192) and prostate cancer mortality (193). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (194). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (195, 196), or depression (197, 198), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (194). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (199). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (200). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (201). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (202-206). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (207). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (208). **Older adults (≥65y)** <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (209). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (210). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (211). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (211). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (212, 213).	

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<td><u>Musculoskeletal conditions</u>
Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (214, 215). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (216, 217). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (218).

<u>Cancer</u>
A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (162).</td>
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<tr>
<td colspan="3">Desirable Effects
How substantial are the desirable anticipated effects?</td>
</tr>
<tr>
<th>JUDGEMENT</th>
<th>RESEARCH EVIDENCE</th>
<th>ADDITIONAL CONSIDERATIONS</th>
</tr>
<tr>
<td>○ Trivial
● Small
○ Moderate
○ Large
○ Varies
○ Don't know</td>
<td><u>Evidence from narrative synthesis</u>:
Only 1 study (219) in people with Spina Bifida was identified. No other RCTs in people with a disability were identified. 1 study (219) unable to be included in a meta-analysis favoured the intervention group. BMI reduced by 2.0 kg/m^2 in the nutrition group versus 1.1 kg/m^2 in the comparator group.

<u>Additional desirable effects</u>:
No additional evidence of desirable effects was identified in this specific population for this intervention.

The following evidence was taken from young and middle-aged adult population.

In nutrition interventions, additional favourable outcomes were improved type 2 diabetes risk (with energy restriction interventions and ad libitum dietary interventions) (75), fasting plasma glucose (very low energy diet [VLED] versus low energy diet [LED]) (220), fasting insulin (with low GI diets) (221), HDL-C (with commercial weight loss programmes (222) and low GI diets (221)), and triglycerides (with commercial weight loss programmes (222)).

For men undertaking nutrition interventions, there were additional beneficial outcomes including increased HDL-C and reduced triglycerides (223).

The following evidence was taken from older adult population.

A review paper (224) found a reduction in total cholesterol for older adults participating in dietary approaches with no specific daily energy intake goal.

<u>Lived experience:</u>
No evidence was identified in this population. The following evidence was taken from the young and middle-aged adult population.</td>
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	Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (225-228). Reduction in mental health symptoms including depression and anxiety (229, 230), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (231-235). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (236-240). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (240-243). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (244-247). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (244, 245). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (199, 223, 248, 249). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (248, 249).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Additional undesirable effects:</u> No additional evidence of undesirable effects was identified in this specific population for this intervention. The following evidence was taken from young and middle-aged adult population. A reported adverse outcome of nutrition interventions was increased fasting plasma glucose with low GI diets (221). <u>Lived experience:</u> No evidence was identified in this population. The following evidence was taken from young and middle-aged adult population. Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (223, 238, 244). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (244, 245). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (249). Fears of embarrassment and failure during exercise activities were also reported (223, 242, 249, 250). Cultural and social expectations related to food and alcohol impacted adherence (238, 242, 251). Limited access to culturally appropriate and healthy foods (242), financial constraints (252), and reluctance to share information with	In adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (256). When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating.

	healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (241, 248, 253-255).	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. The evidence is very uncertain about the effect of this intervention on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with a disability and overweight or obesity in relation to receiving a nutrition treatment. However, the committee believes that since there are benefits, most people with a disability and living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Nutrition interventions are not necessarily widely available and affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours the intervention o Favours the intervention o Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased ● Varies o Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity: Access to healthy food remains inaccessible and/or unaffordable for disadvantaged or remote populations.

		Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of people living with a disability receiving nutrition treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with a disability and overweight or obesity, and clinicians.	Acceptability increases where interventions are individually tailored, inclusive of a range of abilities and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of people living with a disability receiving nutrition interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	**Favours the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:
Dietary approaches with no specific daily energy intake goal may be encouraged as part of a comprehensive approach for management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Froehlich-Grobe K, Lollar D. Obesity and disability: time to act. American Journal of Preventative Medicine. 2011;41(5):541-5. doi: 10.1016/j.amepre.2011.07.015
2. Australian Institute of Health and Welfare. People with disability in Australia 2022: in brief Canberra: Australian Institute of Health and Welfare 2022 [cited 2024 July 22]. Available from: https://www.aihw.gov.au/reports/disability/people-with-disability-in-australia-2022-in-brief.
3. Anderson WL, Wiener JM, Khatutsky G, Armour BS. Obesity and people with disabilities: the implications for health care expenditures. Obesity. 2013;21(12):E798-E804. doi: 10.1002/oby.20531
4. Liao P, Vajdic C, Trollor J, Reppermund S. Prevalence and incidence of physical health conditions in people with intellectual disability – a systematic review. PLoS ONE. 2021;16(8):e0256294. doi: 10.1371/journal.pone.0256294
5. Australian Institute of Health and Welfare. People with disability in Australia Canberra: Australian Institute of Health and Welfare; 2024 [cited 2024 July 22]. Available from: https://www.aihw.gov.au/reports/disability/people-with-disability-in-australia.
6. Ranjan S, Nasser JA, Fisher K. Prevalence and potential factors associated with overweight and obesity status in adults with intellectual developmental disorders. J Appl Res Intellect Disabil. 2018;31(S1):29-38. doi: 10.1111/jar.12370
7. Townsend MJ, Claridy MD, Bajaj SS, Tu L, Stanford FC. Obesity and eligibility for obesity treatments among adults with disabilities in the U.S. Am J Prev Med. 2022;63(4):513-20. doi: 10.1016/j.amepre.2022.04.003
8. McPhee PG, Claridge EA, Noorduyn SG, Gorter JW. Cardiovascular disease and related risk factors in adults with cerebral palsy: a systematic review. Dev Med Child Neurol. 2019;61(8):915-23. doi: 10.1111/dmcn.14028
9. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
10. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
11. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
12. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
13. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
14. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
15. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
16. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
17. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
18. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
19. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
20. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080

21. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
22. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
23. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
24. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
25. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
26. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
27. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
28. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
29. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
30. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
31. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
32. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
33. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
34. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
35. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
36. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
37. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
38. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
39. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
40. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
41. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
42. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
43. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003

44. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
45. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
46. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
47. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
48. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
49. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
50. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
51. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
52. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
53. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
54. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
55. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
56. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
57. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
58. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
59. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
60. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
61. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
62. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
63. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
64. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40

65. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
66. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
67. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
68. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
69. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
70. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
71. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
72. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
73. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
74. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
75. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
76. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
77. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
78. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
79. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
80. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
81. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
82. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
83. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
84. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
85. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
86. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
87. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
88. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
89. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553

90. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
91. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
92. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
93. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
94. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
95. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
96. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
97. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
98. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
99. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
100. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
101. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
102. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
103. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
104. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
105. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
106. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
107. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
108. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
109. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
110. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
111. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
112. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
113. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778

114. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
115. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
116. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
117. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
118. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
119. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
120. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
121. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
122. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
123. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
124. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
125. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
126. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
127. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
128. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
129. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
130. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
131. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
132. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
133. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
134. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
135. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
136. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
137. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232

138. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
139. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
140. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
141. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
142. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
143. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
144. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
145. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
146. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
147. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
148. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
149. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
150. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
151. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
152. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
153. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
154. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
155. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
156. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
157. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
158. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
159. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
160. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
161. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017

162. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
163. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
164. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
165. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
166. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
167. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
168. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
169. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
170. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
171. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
172. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
173. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
174. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
175. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
176. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
177. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
178. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
179. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
180. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
181. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
182. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
183. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
184. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
185. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z

186. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
187. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
188. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
189. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
190. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
191. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
192. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
193. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
194. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
195. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
196. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
197. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
198. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
199. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
200. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
201. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
202. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
203. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
204. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
205. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
206. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
207. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
208. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
209. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002

210. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
211. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
212. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
213. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
214. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
215. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
216. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
217. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
218. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
219. Rendeli C, Kuczynska E, Giuliano AC, Chiaretti A, Ausili E. Dietary approach to prevent obesity risk in Spina Bifida patients. Childs Nerv Syst. 2020;36(7):1515-20. doi: 10.1007/s00381-019-04471-y
220. Huang YS, Zheng Q, Yang H, Fu X, Zhang X, Xia C, et al. Efficacy of intermittent or continuous very low-energy diets in overweight and obese individuals with type 2 diabetes mellitus: a systematic review and meta-analyses. J Diabetes Res. 2020;2020:4851671. doi: 10.1155/2020/4851671
221. Schwingshackl L, Hoffmann G. Long-term effects of low glycemic index/load vs. high glycemic index/load diets on parameters of obesity and obesity-associated risks: a systematic review and meta-analysis. Nutr Metab Cardiovasc Dis. 2013;23(8):699-706. doi: 10.1016/j.numecd.2013.04.008
222. Atallah R, Filion KB, Wakil SM, Genest J, Joseph L, Poirier P, et al. Long-term effects of 4 popular diets on weight loss and cardiovascular risk factors: a systematic review of randomized controlled trials. Circ Cardiovasc Qual Outcomes. 2014;7(6):815-27. doi: 10.1161/CIRCOUTCOMES.113.000723
223. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
224. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. Age Ageing. 2010;39(2):176-84. doi: 10.1093/ageing/afp251
225. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
226. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
227. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
228. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
229. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
230. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752

231. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
232. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
233. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
234. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
235. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
236. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
237. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
238. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
239. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
240. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
241. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
242. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
243. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
244. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
245. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
246. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
247. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
248. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
249. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
250. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
251. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
252. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355

253. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
254. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
255. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227
256. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473

Question: Nutrition interventions compared to treated/untreated comparators for weight maintenance/loss in individuals with a disability experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	Inconsistency	Indirectness	Imprecision	Other considerations			
Nutrition intervention **(dietary approaches with no specific daily energy intake goal) vs untreated comparator (baseline to 12 months)** – narrative synthesis									
1[a]	randomised trials	very serious[b]	not serious	not serious	serious[c]	none	1/1 study favoured the intervention group BMI reduced by 2.0 kg/m² in the nutrition group versus 1.1 kg/m² in the comparator group.	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 1 study, with 1 intervention arm
b. -2 using RoB-2 risk of bias rated High for all outcomes
c. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should interventions combining nutrition and physical activity vs. treated/untreated comparators be used for weight maintenance/loss in individuals with a disability experiencing overweight or obesity?	
POPULATION:	People with a disability living with overweight or obesity
INTERVENTION:	Interventions combining nutrition and physical activity • Combined nutrition and physical activity interventions with or without sedentary behaviour interventions vs any comparator (baseline to 12 months) • Combined nutrition and physical activity interventions vs any comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to Declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Obesity rates are higher among people with disabilities than those without disabilities (1-3). Statistics on people aged ≥2 years living in households in Australia show that the prevalence of overweight and obesity is higher among people with disabilities (72%) than those without disabilities (55%) (2). The disparity between people with and without disabilities in Australia is consistent with international evidence where, for example, the obesity rates of community-dwelling people with disabilities in the US (37%) are much higher than the general population (27%) (3). Obesity can be one aspect of complex health profiles of people with disabilities (4). People with intellectual disability, for example, have high rates of obesity (estimates range from 3.9% to 34.8%) in combination with other physical health conditions, such as epilepsy (9.0% to 51.8%), visual impairment (3.2% to 47.0%), hearing loss (1.4% to 34.9%), osteoporosis (1.7% to 41.0%), cerebral palsy (1.0% to 28.9%), and microcephaly (20.9%) (4). Variations in the ages and intellectual disability severity are likely explanations for the wide ranges in estimates (4). Factors associated with obesity among people with disabilities include poor diet quality (5), low physical activity levels (5), various medications (6), impairment types (6), functional limitations (1), diagnostic overshadowing (7), and environmental barriers (1). Compared with people without disabilities, people with disabilities living in households in Australia had a higher daily consumption of sugar-sweetened beverages (8.3% versus 5.6%) were slightly less likely to be meeting guidelines for fruit and vegetable consumption (45% versus 49%), and more likely to exceed the weekly alcohol consumption guideline (23% versus 19%) (5). Three quarters (74%) of people with disabilities in Australia are not meeting physical activity guidelines, which is similar to those without disability (71%) (5). With respect to medications, many people with intellectual disability, for example, take medications that can cause weight gain, such as second-generation antipsychotics, antidepressants (e.g., Paxil, Zoloft), anticonvulsants (e.g., Depakote), antihypertensives (e.g., Cardura, Inderal), and antidiabetics (e.g., Diabeta, Diabinese) (6). People	72% of Australians with a disability (aged 2 and over) are also living with overweight or obesity, compared with 55% of those without disability (2). 75% Australian males with a disability (aged 2 and over) are living with overweight or obesity. 69% of Australian females with a disability (aged 2 and over) are living with overweight or obesity (2). 79% of older Australians (aged 65 and over) with a disability are also living with overweight or obesity. 68% of younger Australians (aged under 65) with a disability are also living with overweight or obesity (2). 54% Australian adults with disability have hypertension, compared with 27% without a disability. 32% with uncontrolled (or high) blood pressure (2).

	with certain impairments (e.g., Down syndrome) are more susceptible to weight gain (6). Functional limitations can pose barriers to engaging fully in healthy activities, such as physical activity (1). Diagnostic overshadowing can mean that obesity symptoms are overlooked or attributed to patients' impairments, resulting in substandard care for obesity (7). Numerous environmental barriers (e.g., inaccessible environments, fewer health promotion programs accessible for people with disabilities) serve to limit the potential of people with disabilities to engage in activities to prevent or manage overweight and obesity. **People with a disability** Only one systematic review was identified in people with a disability, specifically cerebral palsy. No other reviews of people with other disabilities were identified. The review of cross-sectional and cohort studies in adults with cerebral palsy showed that having overweight or obesity was the most commonly cited cardiovascular disease risk factor (8). While very limited evidence was identified in people with a disability, our review demonstrated a number of health risks associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y). **Children and adolescents (2 to <18y)** <u>Blood pressure indicators</u> Prevalence of prehypertension (9), hypertension and elevated blood pressure (9-14) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (15). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (16, 17). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (9, 12-14). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (15). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (16, 18) and mortality (17, 18) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (17). <u>Blood glucose level</u>	

Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (9, 13, 14). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (13, 14).

<u>Type 2 diabetes mellitus</u>
Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (16-18).

<u>Non-alcoholic fatty liver disease</u>
Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (13) and risk of developing non-alcoholic fatty liver disease (9, 19-21) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (22).

<u>Musculoskeletal conditions</u>
Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (23).

<u>Cancer</u>
Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (24), and ovarian (24, 25) cancer during adulthood among women; and colorectal cancer (26) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (27).

<u>Mental health</u>
Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (13) and depression (13, 28) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (29). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (30).

<u>Health-related quality of life ratings</u>
Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (13). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (31).

Reproductive health

Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (32). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (32). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (32).

Young and middle-aged adults (18 to <65y)

Cardiovascular disease

Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (33-44). Cardiovascular disease mortality increased with increasing weight (43, 45-47). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (48, 49), including ischemic stroke (48), and haemorrhagic stroke (48). Risk was also elevated for coronary artery disease (50, 51).

Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (52). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (53).

Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (37, 54-56).

Blood glucose level

A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (57).

Type 2 diabetes mellitus

Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (41, 51, 58-73).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (37, 57, 74-77).

Non-alcoholic fatty liver disease

Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (78-83).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including

	presence of non-alcoholic steatohepatitis (84-86). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (84). <u>Musculoskeletal conditions</u> Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (87). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (88). <u>Cancer</u> When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (89, 90), thyroid (90-96), and blood cancers such as; lympho-haematopoietic (97) and diffuse large B-cell lymphoma (98, 99), multiple myeloma (90, 99-101), Hodgkin and non-Hodgkin lymphoma (90, 99), and leukemia (102, 103) (obesity only (104)). Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (73, 89, 90, 95, 101, 102, 105-110), gastroesophageal (111, 112), gastric (90, 95, 110, 113, 114), and stomach (73) cancers; and liver (73, 90, 95, 101, 112, 115-124), gallbladder (73, 90, 101, 102, 125-127), bile duct (128), pancreatic (73, 95, 101, 102, 112, 129-131), small intestinal (129), and colorectal (89, 90, 95, 101, 102, 112, 130, 132-149) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (73, 89, 90, 95, 101, 102, 112, 142, 150-154), and bladder (73, 90, 152, 153, 155-158)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (102) cancers, and total cancer risk was associated with increasing adiposity (159). Increased BMI in adulthood (≥18y) was protective against lung cancer (89, 160, 161), and pre-menopausal breast cancer (89, 162). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (163). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (164). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (90, 112, 165-168) (premenopausal (95, 169, 170) or postmenopausal (142) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (171). Risk of other gynaecological cancers also increased, including endometrial (89, 90, 101, 102, 139, 142, 172-175), uterine (73), and cervical cancers (90) (weak association with obesity (176)), as well as breast cancer (95, 102, 112, 139, 142, 159, 176-188). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (52). While some reviews showed that men were at greater risk of prostate-cancer	

	related morbidity or mortality with increasing BMI (152, 189, 190), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (89, 191), while risk increased for development of advanced prostate cancer (112, 153, 191, 192) and prostate cancer mortality (193). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (194). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (195, 196), or depression (197, 198), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (194). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (199). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (200). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (201). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (202-206). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (207). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (208). **Older adults (≥65y)** <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (209). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (210). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (211). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (211). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (212, 213). <u>Musculoskeletal conditions</u>	

	Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (214, 215). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (216, 217). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (218). <u>Cancer</u> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (162).	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Combined nutrition and physical activity (with or without sedentary) behaviour: ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know **Combined nutrition and physical activity (without sedentary behaviour):** ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know **Combined nutrition, physical activity, and sedentary behaviour:** ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from narrative synthesis:</u> 3 studies (219-221) that were unable to be included in a meta-analysis, found a positive effect of combining nutrition and physical activity interventions on weight maintenance/loss. No studies were identified which included a sedentary behaviour intervention. <u>Additional desirable effects:</u> No additional evidence of desirable effects was identified in this specific population for this intervention. The following evidence was taken from the young and middle-aged adult population: Nutrition and physical activity interventions combined, showed favourable effects for cardiovascular events (222), type 2 diabetes risk (223), cancer risk (222), mental health (224), mortality (all cause, cardiovascular, and cancer mortality) (222), systolic (225, 226) and diastolic (226) blood pressure, fasting glucose (225), HbA1c levels (226, 227), and triglycerides (226). Women participating in combined nutrition and physical activity interventions had reduced incidence of type 2 diabetes and reduced systolic blood pressure (228). Additional desirable effects experienced by South Asians participating in combined nutrition and physical activity interventions included reduced diabetes incidence and reduced 2-hour glucose levels (229). Adults with prediabetes participating in combined nutrition and physical activity interventions had reduced incidence of diabetes and improved glycaemic control (230). The following evidence was taken from the older adult population Additional desirable effects experienced by older adults participating in nutrition and physical activity interventions included reduced total cholesterol (231).	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (256), Healthy China Initiative (257), Finnish Diabetes Prevention Study (258)) overwhelmingly support positive health outcomes of physical activity and improved nutrition. The benefits of weight loss or maintenance on cardiometabolic outcomes were also considered when making judgement. In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (259). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (259).

	Lived experience: No evidence was identified in this population. The following evidence was taken from young and middle-aged adult population. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (232-235). Reduction in mental health symptoms including depression and anxiety (224, 236), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (237-241). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (242-246). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (246-249). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (250-253). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (250, 251). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (199, 228, 254, 255). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (254, 255).	
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Combined nutrition and physical activity (with or without sedentary) behaviour: ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know **Combined nutrition and physical activity (without sedentary behaviour):** ● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Additional undesirable effects: No additional evidence of undesirable effects was identified in this specific population for this intervention. The following evidence was taken from the young and middle-aged adult population: Decreased bone mineral density was reported as an adverse outcome experienced when undertaking a nutrition and physical activity intervention (225). Lived experience: No evidence was identified in this population. The following evidence was taken from the young and middle-aged adult population. Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (228, 244, 250). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (250, 251). Engaging in physical activity	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight

Combined nutrition, physical activity, and sedentary behaviour: ● Trivial o Small o Moderate o Large o Varies o Don't know	components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (255). Fears of embarrassment and failure during exercise activities were also reported (228, 248, 255, 260). Cultural and social expectations related to food and alcohol impacted adherence (244, 248, 261). Limited access to culturally appropriate and healthy foods (248), financial constraints (262), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (247, 254, 263-265).	or obesity and a disability, with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
Combined nutrition and physical activity (with or without sedentary) behaviour: ● Very low o Low o Moderate o High o No included studies **Combined nutrition and physical activity (without sedentary behaviour):** ● Very low o Low o Moderate o High o No included studies **Combined nutrition, physical activity, and sedentary behaviour:** ● Very low o Low o Moderate o High o No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. The evidence is very uncertain about the effect of this intervention on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Important uncertainty or variability o Possibly important uncertainty or variability	We have not sourced literature on the preferences and values of people living with a disability and overweight or obesity in relation to receiving a combined nutrition and physical activity treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight

● Probably no important uncertainty or variability ○ No important uncertainty or variability		management.

Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
Combined nutrition and physical activity (with or without sedentary) behaviour: ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know **Combined nutrition and physical activity (without sedentary behaviour):** ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know **Combined nutrition, physical activity, and sedentary behaviour:** ○ Favours the comparison ○ Probably favours the comparison ○ Does not favour	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention. Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention. Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know		

Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition and physical activity interventions are not necessarily widely available and affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Participant-reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	
Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity: Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are often borne by participants, and may be prohibitive for some people, decreasing health equity. Facilities may not be accessible to all participants with a disability. Equity could be addressed by raising the patient’s awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs; or when discussing the patient’s care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Access to NDIS funding and services for eligible patients further addresses equity. Social and health factors are interconnected and complex,

		with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of people living with a disability receiving combined nutrition and physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with a disability and overweight or obesity, and clinicians.	Acceptability increases where interventions are individually tailored inclusive of a range of abilities, and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of people living with a disability receiving combined nutrition and physical activity interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:
Nutrition and physical activity (with or without sedentary behaviour) interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Froehlich-Grobe K, Lollar D. Obesity and disability: time to act. American Journal of Preventative Medicine. 2011;41(5):541-5. doi: 10.1016/j.amepre.2011.07.015
2. Australian Institute of Health and Welfare. People with disability in Australia 2022: in brief Canberra: Australian Institute of Health and Welfare 2022 [cited 2024 July 22]. Available from: https://www.aihw.gov.au/reports/disability/people-with-disability-in-australia-2022-in-brief.
3. Anderson WL, Wiener JM, Khatutsky G, Armour BS. Obesity and people with disabilities: the implications for health care expenditures. Obesity. 2013;21(12):E798-E804. doi: 10.1002/oby.20531
4. Liao P, Vajdic C, Trollor J, Reppermund S. Prevalence and incidence of physical health conditions in people with intellectual disability – a systematic review. PLoS ONE. 2021;16(8):e0256294. doi: 10.1371/journal.pone.0256294
5. Australian Institute of Health and Welfare. People with disability in Australia Canberra: Australian Institute of Health and Welfare; 2024 [cited 2024 July 22]. Available from: https://www.aihw.gov.au/reports/disability/people-with-disability-in-australia.
6. Ranjan S, Nasser JA, Fisher K. Prevalence and potential factors associated with overweight and obesity status in adults with intellectual developmental disorders. J Appl Res Intellect Disabil. 2018;31(S1):29-38. doi: 10.1111/jar.12370
7. Townsend MJ, Claridy MD, Bajaj SS, Tu L, Stanford FC. Obesity and eligibility for obesity treatments among adults with disabilities in the U.S. Am J Prev Med. 2022;63(4):513-20. doi: 10.1016/j.amepre.2022.04.003
8. McPhee PG, Claridge EA, Noorduyn SG, Gorter JW. Cardiovascular disease and related risk factors in adults with cerebral palsy: a systematic review. Dev Med Child Neurol. 2019;61(8):915-23. doi: 10.1111/dmcn.14028
9. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
10. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
11. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
12. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
13. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
14. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
15. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
16. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
17. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
18. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
19. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
20. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
21. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010

22. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
23. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
24. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
25. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
26. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
27. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
28. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
29. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
30. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
31. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
32. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
33. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
34. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
35. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
36. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
37. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
38. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
39. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
40. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
41. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
42. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
43. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
44. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948

45. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
46. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
47. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
48. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
49. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
50. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
51. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
52. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
53. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
54. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
55. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
56. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
57. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
58. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
59. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
60. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
61. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
62. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
63. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
64. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
65. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3

66. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
67. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
68. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
69. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
70. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
71. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
72. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
73. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
74. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
75. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
76. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
77. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
78. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
79. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
80. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
81. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
82. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
83. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
84. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
85. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
86. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
87. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
88. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
89. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
90. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824

91. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
92. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
93. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
94. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
95. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
96. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
97. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
98. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
99. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
100. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
101. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
102. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
103. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
104. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
105. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
106. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
107. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
108. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
109. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
110. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
111. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
112. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
113. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
114. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042

115. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
116. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
117. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
118. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
119. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
120. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
121. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
122. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
123. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
124. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
125. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
126. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
127. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
128. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
129. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
130. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
131. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
132. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
133. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
134. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
135. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
136. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
137. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
138. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945

139. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
140. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
141. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
142. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
143. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
144. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
145. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
146. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
147. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
148. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
149. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
150. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
151. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
152. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
153. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
154. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
155. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
156. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
157. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
158. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
159. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
160. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
161. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017

162. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
163. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
164. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
165. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
166. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
167. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
168. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
169. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
170. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
171. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
172. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
173. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
174. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
175. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
176. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
177. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
178. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
179. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
180. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
181. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
182. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
183. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
184. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
185. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z

186. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
187. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
188. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
189. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
190. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
191. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
192. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
193. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
194. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
195. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
196. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
197. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
198. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
199. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
200. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
201. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
202. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
203. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
204. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
205. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
206. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
207. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
208. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
209. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002

210. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
211. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
212. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
213. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
214. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
215. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
216. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
217. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
218. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
219. Harris L, Hankey C, Jones N, Pert C, Murray H, Tobin J, et al. A cluster randomised control trial of a multi-component weight management programme for adults with intellectual disabilities and obesity. Br J Nutr. 2017;118(3):229-40. doi: 10.1017/S0007114517001933
220. Reichard A, Saunders MD, Saunders RR, Donnelly JE, Lauer E, Sullivan DK, Ptomey L. A comparison of two weight management programs for adults with mobility impairments. Disabil Health J. 2015;8(1):61-9. doi: 10.1016/j.dhjo.2014.08.002
221. Yadav V, Marracci G, Kim E, Spain R, Cameron M, Overs S, et al. Low-fat, plant-based diet in multiple sclerosis: a randomized controlled trial. Mult Scler Relat Disord. 2016;9:80-90. doi: 10.1016/j.msard.2016.07.001
222. Ma C, Avenell A, Bolland M, Hudson J, Stewart F, Robertson C, et al. Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease, and cancer: systematic review and meta-analysis. BMJ. 2017;359:j4849. doi: 10.1136/bmj.j4849
223. LeBlanc ES, Patnode CD, Webber EM, Redmond N, Rushkin M, O'Connor EA. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2018;320(11):1172-91. doi: 10.1001/jama.2018.7777
224. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
225. Leblanc ES, O'Connor E, Whitlock EP, Patnode CD, Kapka T. Effectiveness of primary care-relevant treatments for obesity in adults: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2011;155(7):434-47. doi: 10.7326/0003-4819-155-7-201110040-00006
226. Dombrowski SU, Avenell A, Sniehott FF. Behavioural interventions for obese adults with additional risk factors for morbidity: systematic review of effects on behaviour, weight and disease risk factors. Obes Facts. 2010;3(6):377-96. doi: 10.1159/000323076
227. Johnson M, Jones R, Freeman C, Woods HB, Gillett M, Goyder E, Payne N. Can diabetes prevention programmes be translated effectively into real-world settings and still deliver improved outcomes? A synthesis of evidence. Diabet Med. 2013;30(1):3-15. doi: 10.1111/dme.12018
228. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
229. Jenum AK, Brekke I, Mdala I, Muilwijk M, Ramachandran A, Kjøllesdal M, et al. Effects of dietary and physical activity interventions on the risk of type 2 diabetes in South Asians: meta-analysis of individual participant data from randomised controlled trials. Diabetologia. 2019;62(8):1337-48. doi: 10.1007/s00125-019-4905-2
230. Kerrison G, Gillis RB, Jiwani SI, Alzahrani Q, Kok S, Harding SE, et al. The effectiveness of lifestyle adaptation for the prevention of prediabetes in adults: a systematic review. J Diabetes Res. 2017;2017:8493145. doi: 10.1155/2017/8493145
231. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. Age Ageing. 2010;39(2):176-84. doi: 10.1093/ageing/afp251

232. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
233. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
234. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
235. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
236. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
237. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
238. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
239. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
240. Palavras MA, Hay P, Filho CADS, Claudino A. The fficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
241. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
242. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
243. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
244. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
245. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
246. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
247. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
248. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
249. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
250. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
251. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
252. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132

253. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
254. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
255. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
256. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
257. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
258. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
259. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
260. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
261. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
262. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
263. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
264. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
265. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition and physical activity compared to treated/untreated comparators for weight maintenance/loss in individuals with a disability experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	interventions **combining nutrition and physical activity**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Combined nutrition and physical activity interventions with or without sedentary behaviour vs any comparator (baseline to 12 months) – narrative synthesis												
3[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	3/3 studies found a positive effect of combining nutrition and physical activity interventions on weight maintenance/loss				⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 3 studies, with 3 intervention arms
b. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
c. -1 due to unspecified heterogeneity due to differences in exposure
d. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should interventions combining nutrition, physical activity and family-centred vs. treated/untreated comparators be used for weight maintenance/loss in individuals with a disability experiencing overweight or obesity?	
POPULATION:	People with a disability living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and family-centred interventions vs any comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Obesity rates are higher among people with disabilities than those without disabilities (1-3). Statistics on people aged ≥2 years living in households in Australia show that the prevalence of overweight and obesity is higher among people with disabilities (72%) than those without disabilities (55%) (2). The disparity between people with and without disabilities in Australia is consistent with international evidence where, for example, the obesity rates of community-dwelling people with disabilities in the US (37%) are much higher than the general population (27%) (3). Obesity can be one aspect of complex health profiles of people with disabilities (4). People with intellectual disability, for example, have high rates of obesity (estimates range from 3.9% to 34.8%) in combination with other physical health conditions, such as epilepsy (9.0% to 51.8%), visual impairment (3.2% to 47.0%), hearing loss (1.4% to 34.9%), osteoporosis (1.7% to 41.0%), cerebral palsy (1.0% to 28.9%), and microcephaly (20.9%) (4). Variations in the ages and intellectual disability severity are likely explanations for the wide ranges in estimates (4). Factors associated with obesity among people with disabilities include poor diet quality (5), low physical activity levels (5), various medications (6), impairment types (6), functional limitations (1), diagnostic overshadowing (7), and environmental barriers (1). Compared with people without disabilities, people with disabilities living in households in Australia had a higher daily consumption of sugar-sweetened beverages (8.3% versus 5.6%) were slightly less likely to be meeting guidelines for fruit and vegetable consumption (45% versus 49%), and more likely to exceed the weekly alcohol consumption guideline (23% versus 19%) (5). Three quarters (74%) of people with disabilities in Australia are not meeting physical activity guidelines, which is similar to those without disability (71%) (5). With respect to medications, many people with intellectual disability, for example, take medications that can cause weight gain, such as second-generation antipsychotics, antidepressants (e.g., Paxil, Zoloft), anticonvulsants (e.g., Depakote), antihypertensives (e.g., Cardura, Inderal), and antidiabetics (e.g., Diabeta, Diabinese) (6). People with certain impairments (e.g., Down syndrome) are more susceptible to weight gain (6). Functional limitations can pose barriers to	72% of Australians with a disability (aged 2 and over) are also living with overweight or obesity, compared with 55% of those without disability (2). 75% Australian males with a disability (aged 2 and over) are living with overweight or obesity. 69% of Australian females with a disability (aged 2 and over) are living with overweight or obesity (2). 79% of older Australians (aged 65 and over) with a disability are also living with overweight or obesity. 68% of younger Australians (aged under 65) with a disability are also living with overweight or obesity (2). 54% Australian adults with disability have hypertension, compared with 27% without a disability. 32% with uncontrolled (or high) blood pressure (2).

	engaging fully in healthy activities, such as physical activity (1). Diagnostic overshadowing can mean that obesity symptoms are overlooked or attributed to patients' impairments, resulting in substandard care for obesity (7). Numerous environmental barriers (e.g., inaccessible environments, fewer health promotion programs accessible for people with disabilities) serve to limit the potential of people with disabilities to engage in activities to prevent or manage overweight and obesity. **People with a disability** Only one systematic review was identified in people with a disability, specifically cerebral palsy. No other reviews of people with other disabilities were identified. The review of cross-sectional and cohort studies in adults with cerebral palsy showed that having overweight or obesity was the most commonly cited cardiovascular disease risk factor (8). While very limited evidence was identified in people with a disability, our review demonstrated a number of health risks associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y). **Children and adolescents (2 to <18y)** <u>Blood pressure indicators</u> Prevalence of prehypertension (9), hypertension and elevated blood pressure (9-14) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (15). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (16, 17). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (9, 12-14). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (15). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (16, 18) and mortality (17, 18) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (17). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with	

healthy weight (9, 13, 14). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (13, 14).

Type 2 diabetes mellitus

Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (16-18).

Non-alcoholic fatty liver disease

Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (13) and risk of developing non-alcoholic fatty liver disease (9, 19-21) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (22).

Musculoskeletal conditions

Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (23).

Cancer

Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (24), and ovarian (24, 25) cancer during adulthood among women; and colorectal cancer (26) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (27).

Mental health

Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (13) and depression (13, 28) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (29). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (30).

Health-related quality of life ratings

Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (13). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (31).

Reproductive health

Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (32). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (32). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (32).

Young and middle-aged adults (18 to <65y)

<u>Cardiovascular disease</u>

Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (33-44). Cardiovascular disease mortality increased with increasing weight (43, 45-47). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (48, 49), including ischemic stroke (48), and haemorrhagic stroke (48). Risk was also elevated for coronary artery disease (50, 51).

Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or ‘other’ causes, compared to healthy weight survivors (52). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (53).

Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants’ risk of mortality from cardiovascular disease decreased (37, 54-56).

<u>Blood glucose level</u>

A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (57).

<u>Type 2 diabetes mellitus</u>

Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (41, 51, 58-73).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (37, 57, 74-77).

<u>Non-alcoholic fatty liver disease</u>

Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (78-83).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (84-86). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (84).

Musculoskeletal conditions

Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (87). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (88).

Cancer

When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (89, 90), thyroid (90-96), and blood cancers such as; lympho-haematopoietic (97) and diffuse large B-cell lymphoma (98, 99), multiple myeloma (90, 99-101), Hodgkin and non-Hodgkin lymphoma (90, 99), and leukemia (102, 103) (obesity only (104)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (73, 89, 90, 95, 101, 102, 105-110), gastroesophageal (111, 112), gastric (90, 95, 110, 113, 114), and stomach (73) cancers; and liver (73, 90, 95, 101, 112, 115-124), gallbladder (73, 90, 101, 102, 125-127), bile duct (128), pancreatic (73, 95, 101, 102, 112, 129-131), small intestinal (129), and colorectal (89, 90, 95, 101, 102, 112, 130, 132-149) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (73, 89, 90, 95, 101, 102, 112, 142, 150-154), and bladder (73, 90, 152, 153, 155-158)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (102) cancers, and total cancer risk was associated with increasing adiposity (159). Increased BMI in adulthood (≥18y) was protective against lung cancer (89, 160, 161), and pre-menopausal breast cancer (89, 162). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (163). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (164).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (90, 112, 165-168) (premenopausal (95, 169, 170) or postmenopausal (142) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (171). Risk of other gynaecological cancers also increased, including endometrial (89, 90, 101, 102, 139, 142, 172-175), uterine (73), and cervical cancers (90) (weak association with obesity (176)), as well as breast cancer (95, 102, 112, 139, 142, 159, 176-188). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (52). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (152, 189, 190), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (89, 191), while risk increased for development of advanced prostate cancer (112, 153, 191, 192) and prostate cancer mortality (193).

<u>Mental health</u>
Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (194). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (195, 196), or depression (197, 198), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (194).

<u>Health-related quality of life ratings</u>
Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (199).

<u>Reproductive health</u>
Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (200). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (201). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (202-206).

Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (207). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (208).

Older adults (≥65y)
<u>Cardiovascular disease</u>
The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (209). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (210).
Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (211). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (211).

<u>Type 2 diabetes mellitus</u>
Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (212, 213).

<u>Musculoskeletal conditions</u>
Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI

	had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (214, 215). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (216, 217). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (218). <u>Cancer</u> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (162).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analyses:</u> From 2 studies (219, 220) with 71 intervention participants and 42 comparator participants, evidence demonstrated a moderate effect size of Hedges' g 0.68 lower (2.12 lower to 0.76 higher) in the nutrition, physical activity and family-centred intervention versus comparator. No additional evidence of desirable effects was identified in this specific population for this intervention. <u>Lived Experience</u> No evidence was found in this population. The following evidence was taken from young and middle-aged adult population. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (221-224). Reduction in mental health symptoms including depression and anxiety (225, 226), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (227-231). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (232-235). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (235-238). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (239-242). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (239, 240). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (199, 243-245). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (244, 245).	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (246), Healthy China Initiative (247), Finnish Diabetes Prevention Study (248)) overwhelmingly support positive health outcomes of physical activity and improved nutrition. The benefits of weight loss or maintenance on cardiometabolic outcomes were also considered when making judgement. In adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (249). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass. (249).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No evidence of undesirable effects was identified in this specific population for this intervention. Lived Experience No evidence was identified in this population. The following evidence was taken from young and middle-aged adult population. Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (234, 239, 243). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (239, 240). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (245). Fears of embarrassment and failure during exercise activities were also reported (237, 243, 245, 250). Cultural and social expectations related to food and alcohol impacted adherence (234, 237, 251). Limited access to culturally appropriate and healthy foods (237), financial constraints (252), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (236, 244, 253-255).	When people with a disability who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change, increased physical activity, and is family-centred, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity and a disability during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity and a disability, with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. The evidence is very uncertain about the effect of this intervention on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or	We have not sourced literature on the preferences and values of people living with a disability and overweight or obesity in relation to receiving a	Some people living with overweight or obesity,

variability o Possibly important uncertainty or variability ● Probably no important uncertainty or variability o No important uncertainty or variability	combined nutrition, physical activity, and family-centred treatment. However, the committee believes that since there are benefits, most people with a disability who are living with overweight or obesity, including those living with a disability and/or their caregivers, would opt for this treatment.	(possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favours the intervention o Varies o Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Large costs o Moderate costs o Negligible costs and savings o Moderate savings o Large savings o Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition, physical activity and family-centred interventions are not necessarily widely available and affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Participant-reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity: Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are often borne by participants, and may be prohibitive for some people, decreasing health equity. Facilities may not be accessible to all participants with a disability. Equity could be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity

		programs; or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Access to NDIS funding and services for eligible patients further addresses equity. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of people living with a disability receiving combined nutrition, physical activity, and family-centred treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with a disability and overweight or obesity, and clinicians.	Acceptability increases where interventions are individually tailored, inclusive of a range of abilities, and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no	Literature on the feasibility of people living with a disability receiving combined nutrition, physical activity and family-centred interventions was	Resourcing will be dependent on setting, intervention,

● Probably yes ○ Yes ○ Varies ○ Don't know	not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:
Combined nutrition, physical activity and family-centred interventions may be encouraged as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Froehlich-Grobe K, Lollar D. Obesity and disability: time to act. American Journal of Preventative Medicine. 2011;41(5):541-5. doi: 10.1016/j.amepre.2011.07.015
2. Australian Institute of Health and Welfare. People with disability in Australia 2022: in brief Canberra: Australian Institute of Health and Welfare 2022 [cited 2024 July 22]. Available from: https://www.aihw.gov.au/reports/disability/people-with-disability-in-australia-2022-in-brief.
3. Anderson WL, Wiener JM, Khatutsky G, Armour BS. Obesity and people with disabilities: the implications for health care expenditures. Obesity. 2013;21(12):E798-E804. doi: 10.1002/oby.20531
4. Liao P, Vajdic C, Trollor J, Reppermund S. Prevalence and incidence of physical health conditions in people with intellectual disability – a systematic review. PLoS ONE. 2021;16(8):e0256294. doi: 10.1371/journal.pone.0256294
5. Australian Institute of Health and Welfare. People with disability in Australia Canberra: Australian Institute of Health and Welfare; 2024 [cited 2024 July 22]. Available from: https://www.aihw.gov.au/reports/disability/people-with-disability-in-australia.
6. Ranjan S, Nasser JA, Fisher K. Prevalence and potential factors associated with overweight and obesity status in adults with intellectual developmental disorders. J Appl Res Intellect Disabil. 2018;31(S1):29-38. doi: 10.1111/jar.12370
7. Townsend MJ, Claridy MD, Bajaj SS, Tu L, Stanford FC. Obesity and eligibility for obesity treatments among adults with disabilities in the U.S. Am J Prev Med. 2022;63(4):513-20. doi: 10.1016/j.amepre.2022.04.003
8. McPhee PG, Claridge EA, Noorduyn SG, Gorter JW. Cardiovascular disease and related risk factors in adults with cerebral palsy: a systematic review. Dev Med Child Neurol. 2019;61(8):915-23. doi: 10.1111/dmcn.14028
9. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
10. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
11. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
12. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
13. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
14. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
15. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
16. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
17. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
18. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
19. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
20. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080

21. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
22. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
23. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
24. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
25. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
26. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
27. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
28. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
29. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
30. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
31. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
32. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
33. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
34. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
35. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
36. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
37. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
38. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
39. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
40. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
41. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
42. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
43. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003

44. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
45. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
46. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
47. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
48. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
49. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
50. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
51. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
52. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
53. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
54. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
55. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
56. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
57. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
58. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
59. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
60. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
61. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
62. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
63. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
64. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40

65. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
66. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
67. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
68. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
69. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
70. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
71. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
72. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
73. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
74. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
75. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
76. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
77. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
78. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
79. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
80. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
81. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
82. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
83. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
84. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
85. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
86. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
87. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
88. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
89. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553

90. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
91. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
92. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
93. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
94. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
95. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
96. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
97. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
98. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
99. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
100. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
101. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
102. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
103. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
104. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
105. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
106. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
107. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
108. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
109. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
110. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
111. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
112. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
113. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778

114. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
115. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
116. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
117. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
118. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
119. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
120. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
121. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
122. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
123. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
124. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
125. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
126. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
127. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
128. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
129. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
130. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
131. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
132. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
133. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
134. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
135. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
136. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
137. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232

138. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
139. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
140. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
141. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
142. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
143. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
144. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
145. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
146. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
147. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
148. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
149. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
150. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
151. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
152. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
153. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
154. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
155. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
156. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
157. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
158. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
159. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
160. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
161. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017

162. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
163. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
164. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
165. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
166. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
167. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
168. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
169. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
170. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
171. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
172. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
173. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
174. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
175. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
176. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
177. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
178. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
179. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
180. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
181. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
182. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
183. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
184. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
185. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z

186. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
187. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
188. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
189. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
190. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
191. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
192. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
193. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
194. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
195. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
196. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
197. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
198. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
199. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
200. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
201. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
202. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
203. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
204. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
205. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
206. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
207. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
208. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
209. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002

210. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
211. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
212. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
213. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
214. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
215. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
216. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
217. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
218. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
219. Curtin C, Bandini LG, Must A, Gleason J, Lividini K, Phillips S, et al. Parent support improves weight loss in adolescents and young adults with Down syndrome. J Pediatr. 2013;163(5):1402-8.e1. doi: 10.1016/j.jpeds.2013.06.081
220. Ptomey LT, Washburn RA, Goetz JR, Sullivan DK, Gibson CA, Mayo MS, et al. A randomized trial comparing diet and delivery strategies for weight management in adolescents with intellectual disabilities. Pediatr Obes. 2023;18(1):e12972. doi: 10.1111/ijpo.12972
221. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
222. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
223. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
224. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
225. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
226. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
227. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
228. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
229. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
230. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299

231. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
232. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
233. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
234. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
235. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
236. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
237. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
238. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
239. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
240. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
241. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
242. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
243. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
244. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
245. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
246. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
247. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
248. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
249. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
250. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
251. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
252. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
253. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347

254. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x

255. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition, physical activity and family-centred compared to treated/untreated comparators for weight maintenance/loss in individuals with a disability experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	interventions **combining nutrition, physical activity and family-centred**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Combined nutrition, physical activity, and family-centred interventions vs any comparator (baseline to 12 months)												
2[a]	randomised trials	very serious[b]	serious[c]	not serious	serious[d]	none	71	42	-	Hedges' g 0.68 **lower** (2.12 lower to 0.76 higher)	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 2 studies, 3 intervention arms
b. -2 using RoB-2 risk of bias rated Some concerns (1 (9%) outcomes), High (10 (91%) outcomes)
c. -1 Inconsistency of I^2= 62.49%
d. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)

People with a mental health condition

QUESTION

Should Interventions combining nutrition and physical activity with or without sedentary behaviour vs. treated/untreated comparators be used for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity?	
POPULATION:	People with a mental health condition living with overweight or obesity. Studies included in this analysis included participants who had serious mental illness (i.e. schizophrenia, schizoaffective disorder, bipolar disorder, or posttraumatic stress disorder with psychotic symptoms) and prescribed an antipsychotic [i.e. olanzapine/clozapine (high weight-gain risk), risperidone/quetiapine (medium weight-gain risk), aripiprazole/ziprasidone (low weight-gain risk), lithium or other mood stabilisers or 'other' antipsychotics].
INTERVENTION:	Interventions combining nutrition and physical activity with or without sedentary behaviour: • Combined nutrition and physical activity interventions vs untreated comparator (baseline to 12 months). No interventions with sedentary behaviour components were identified.
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Mental health conditions increase the propensity for developing obesity (1, 2). People with severe mental illness (e.g., schizophrenia, bipolar disorder affective disorder, major depressive disorder with psychosis) have three times higher odds of obesity than the general population (OR=3.04; 95% CI: 2.42, 3.82) (1). The odds of overweight are equivalent, however (OR=1.07; 95% CI: 0.91, 1.27) (1). Among people with schizophrenia, woman have higher odds of overweight (OR=1.27; 95% CI: 1.16, 1.39) and obesity (OR=1.46; 95% CI: 1.23, 1.72) than men (1). Similarly, people with depression (symptoms and disorder) have higher odds of developing obesity (OR=1.58; 95% CI: 1.33, 1.87) but not overweight (OR=1.20, 95% CI: 0.87, 1.66) (2). Factors contributing to obesity among people with mental health conditions include poor quality diets and eating patterns (3), sedentary behaviour and low physical activity levels (4), and psychotropic medications (5). People with severe mental illness consume more dietary energy (mean difference=1332kJ; 95% CI: 487, 2178) and sodium (mean difference=322mg; 95% CI: 174, 490) than healthy controls (3). The diets of people with severe mental illness tend to be less healthy, with low consumption of fruit and vegetables and high intakes of sugar-sweetened beverages and takeaway and other convenience foods (3). Compared to healthy controls, people with severe mental illness are more sedentary (mean difference=10.1mins/day; 95% CI: 1.9, 22.2) and less engaged in moderate physical activity (mean difference=10.2mins/day; 95% CI: 3.2,	

17.2) and vigorous physical activity (mean difference=3.2mins/day; 95% CI: 1.1, 6.4) (4). Weight-gain is a side-effect of nearly all antipsychotic medications, with two second-generation antipsychotics (clozapine and olanzapine) having the greatest potential to produce increases in weight (5). There is a moderate risk of weight gain with other second-generation anti-psychotics (quetiapine, risperidone, paliperidone and iloperidone) (5). The potential for weight gain also exists with first-generation antipsychotics (e.g., chlorpromazine and thioridazine), antidepressants (e.g., amitriptyline, mirtazapine, and paroxetine), and mood stabilizers (lithium, valproate) (5).

A number of health risks are associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y).

Children and adolescents (2 to <18y)

<u>Blood pressure indicators</u>

Prevalence of prehypertension (6), hypertension and elevated blood pressure (6-11) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (12). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (13, 14).

<u>Blood lipid profile</u>

Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (6, 9-11). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (12).

<u>Cardiovascular disease</u>

Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (13, 15) and mortality (14, 15) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (14).

<u>Blood glucose level</u>

Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (6, 10, 11). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (10, 11).

<u>Type 2 diabetes mellitus</u>

Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated

	with an increased risk of developing Type 2 diabetes mellitus in adulthood (13-15). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (10) and risk of developing non-alcoholic fatty liver disease (6, 16-18) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (19). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (20). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (21), and ovarian (21, 22) cancer during adulthood among women; and colorectal cancer (23) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (24). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (10) and depression (10, 25) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (26). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (27). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (10). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (28). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (29). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (29). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (29).	

	Young and middle-aged adults (18 to <65y) Cardiovascular disease Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (30-41). Cardiovascular disease mortality increased with increasing weight (40, 42-44). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (45, 46), including ischemic stroke (45), and haemorrhagic stroke (45). Risk was also elevated for coronary artery disease (47, 48). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (49). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (50). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (34, 51-53). Blood glucose level A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (54). Type 2 diabetes mellitus Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (38, 48, 55-70). Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (34, 54, 71-74). Non-alcoholic fatty liver disease Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (75-80). Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (81-83). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (81). Musculoskeletal conditions Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (84). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (85).	

	<u>Cancer</u> When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (86, 87), thyroid (87-93), and blood cancers such as; lympho-haematopoietic (94) and diffuse large B-cell lymphoma (95, 96), multiple myeloma (87, 96-98), Hodgkin and non-Hodgkin lymphoma (87, 96), and leukemia (99, 100) (obesity only (101)). Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (70, 86, 87, 92, 98, 99, 102-107), gastroesophageal (108, 109), gastric (87, 92, 107, 110, 111), and stomach (70) cancers; and liver (70, 87, 92, 98, 109, 112-121), gallbladder (70, 87, 98, 99, 122-124), bile duct (125), pancreatic (70, 92, 98, 99, 109, 126-128), small intestinal (126), and colorectal (86, 87, 92, 98, 99, 109, 127, 129-146) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (70, 86, 87, 92, 98, 99, 109, 139, 147-151), and bladder (70, 87, 149, 150, 152-155)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (99) cancers, and total cancer risk was associated with increasing adiposity (156). Increased BMI in adulthood (≥18y) was protective against lung cancer (86, 157, 158), and pre-menopausal breast cancer (86, 159). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (160). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (161). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (87, 109, 162-165) (premenopausal (92, 166, 167) or postmenopausal (139) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (168). Risk of other gynaecological cancers also increased, including endometrial (86, 87, 98, 99, 136, 139, 169-172), uterine (70), and cervical cancers (87) (weak association with obesity (173)), as well as breast cancer (92, 99, 109, 136, 139, 156, 173-185). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (49). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (149, 186, 187), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (86, 188), while risk increased for development of advanced prostate cancer (109, 150, 188, 189) and prostate cancer mortality (190). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (191). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (192, 193), or depression (194, 195), including significant increases in	

	depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (191). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (196). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (197). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (198). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (199-203). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (204). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (205). **Older adults (≥65y)** <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (206). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (207). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (208). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (208). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (209, 210). <u>Musculoskeletal conditions</u> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (211, 212). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (213, 214). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (215). <u>Cancer</u> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (159).	

Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from narrative synthesis: 2 studies (216, 217) that were unable to be included in a meta-analysis found a positive effect of combining nutrition and physical activity interventions on weight maintenance/loss. Additional desirable effects: No evidence available in people with mental health condition. The following evidence was derived from general young and middle-aged adults. Nutrition and physical activity interventions combined, showed favourable effects for cardiovascular events (218), type 2 diabetes risk (219), cancer risk (218), mental health (220), mortality (all cause, cardiovascular, and cancer mortality) (218), systolic (221, 222) and diastolic (222) blood pressure, fasting glucose (221), HbA1c levels (222, 223), and triglycerides (222). Women participating in combined nutrition and physical activity interventions had reduced incidence of type 2 diabetes and reduced systolic blood pressure (224). Additional desirable effects experienced by South Asians participating in combined nutrition and physical activity interventions included reduced diabetes incidence and reduced 2-hour glucose levels (225). Adults with prediabetes participating in combined nutrition and physical activity interventions had reduced incidence of diabetes and improved glycaemic control (226). The below evidence was derived from the general older adult population. Additional desirable effects experienced by older adults participating in nutrition and physical activity interventions included reduced total cholesterol (227). Lived experience: One review paper (228) reported the experiences of people with serious mental illness. Participants reported improved self-esteem and self-efficacy outcomes after nutrition and physical activity programmes that emphasized successes and praised achievements in a non-judgmental and supportive environment (228). Programs tailored to the challenges of mental health conditions (e.g., shorter, repeated sessions with regular breaks, call reminders) supported engagement and attendance (228). The following evidence was taken from studies of young and middle-aged adult populations. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (229-232). Reduction in mental health symptoms including depression and anxiety (220, 233), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (234-238). Social support and	Research findings from multiple, large community-based longitudinal studies (e.g. the Diabetes Prevention Program (USA) (253), Healthy China Initiative (254), Finnish Diabetes Prevention Study (255)) overwhelmingly support positive health outcomes of physical activity. The benefits of weight loss or maintenance on cardiometabolic outcomes were also considered when making judgement. In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (256). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (256).

	positive engagement from programme facilitators were shown to influence successful behaviour change (239-243). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (243-246). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (247-250). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (247, 248). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (196, 224, 251, 252). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (251, 252).	
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from meta-analysis: No evidence was identified in this population. Additional undesirable effects: No evidence available in people with mental health conditions, evidence derived from general young and middle-aged adults. Decreased bone mineral density was reported as an adverse outcome experienced when undertaking a nutrition and physical activity intervention (221). Lived experience: One review paper (228) reported the experiences of people with serious mental illness. This group experiences several barriers to behavioural weight management programs. People with mental health conditions reported difficulty initiating and adhering to weight maintenance/loss programs because of fluctuating symptoms and medication side effects, that in turn caused varying motivation, ability, and added stressors to support networks (228). Some medications may affect the ability to manage weight, which may contribute to lower self-esteem. Structural barriers may include prohibitive cost of or inaccessibility of food, gym memberships or equipment, and transport (228). The following evidence was taken from young and middle-aged adult population: Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (224, 241, 247). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (247, 248). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using	When people who are living with overweight or obesity and a mental illness are participating in a behavioural weight loss intervention that incorporates diet change, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity and a mental illness, with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs

	equipment that was not suitable for their body size (252). Fears of embarrassment and failure during exercise activities were also reported (224, 245, 252, 257). Cultural and social expectations related to food and alcohol impacted adherence (241, 245) (258). Limited access to culturally appropriate and healthy foods (245), financial constraints (228), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (244, 251, 259-261).	to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. The evidence is very uncertain about the effect of this intervention on adiposity.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with a mental health condition and overweight or obesity in relation to receiving combined nutrition and physical activity treatment. However, the committee believes that since there are benefits, most people with mental health conditions and overweight or obesity, and clinicians would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● Don't know	Limited research evidence was identified, however, given the effectiveness of multimodal interventions for the adult population, the committee has reached a consensus decision that the balance between the desirable and undesirable effects is unknown.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition and physical activity interventions are not necessarily widely available and affordable.	Financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing, were reported. Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	From a societal perspective, a 6-month nutrition and physical activity intervention for adults with serious mental illness taking antipsychotic medications and with BMI≥27 costed $US2,042 per 1kg of weight loss (262). The societal perspective included intervention delivery, recruitment, and participant costs, and savings from reduced hospitalisations.	

Equity
What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Access to healthy food remains inaccessible and/or unaffordable for disadvantaged or remote populations. High costs of gym memberships, sporting club fees and equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. Local knowledge is important for increasing accessibility to low-cost physical activity options. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with Indigenous People or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions

		for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of people living with a mental health condition receiving combined nutrition and physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with a mental health condition and overweight or obesity, and clinicians.	Acceptability increases where nutrition and physical activity interventions are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of people living with a mental health condition receiving combined nutrition and physical activity interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**Don't know**
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Combined nutrition and physical activity interventions may be encouraged as part of a comprehensive approach to management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Afzal M, Siddiqi N, Ahmad B, Afsheen N, Aslam F, Ali A, et al. Prevalence of overweight and obesity in people with severe mental illness: systematic review and meta-analysis. Front Endocrinol. 2021;12. doi: 10.3389/fendo.2021.769309
2. Luppino FS, De Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BWJH, Zitman FG. Overweight, obesity, and depression. Arch Gen Psychiatry. 2010;67(3):220. doi: 10.1001/archgenpsychiatry.2010.2
3. Teasdale SB, Ward PB, Samaras K, Firth J, Stubbs B, Tripodi E, Burrows TL. Dietary intake of people with severe mental illness: systematic review and meta-analysis. Br J Psychiatry. 2019;214(5):251-9. doi: 10.1192/bjp.2019.20
4. Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, et al. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. World Psychiatry. 2017;16(3):308-15. doi: 10.1002/wps.20458
5. Mazereel V, Detraux J, Vancampfort D, Van Winkel R, De Hert M. Impact of psychotropic medication effects on obesity and the metabolic syndrome in people with serious mental illness. Front Endocrinol. 2020;11. doi: 10.3389/fendo.2020.573479
6. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
7. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
8. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
9. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
10. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
11. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
12. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
13. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
14. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
15. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
16. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
17. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
18. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
19. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
20. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067

21. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
22. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
23. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
24. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
25. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
26. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
27. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
28. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
29. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
30. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
31. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
32. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
33. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
34. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
35. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
36. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
37. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
38. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
39. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
40. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
41. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
42. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
43. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247

44. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
45. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
46. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
47. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
48. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
49. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
50. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
51. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
52. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
53. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
54. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
55. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
56. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
57. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
58. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
59. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
60. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
61. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
62. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
63. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
64. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
65. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218

66. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
67. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
68. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
69. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
70. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
71. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
72. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
73. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
74. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
75. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
76. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
77. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
78. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
79. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
80. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
81. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
82. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
83. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
84. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
85. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
86. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
87. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
88. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
89. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
90. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
91. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321

92. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
93. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
94. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
95. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
96. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
97. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
98. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
99. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
100. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
101. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
102. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
103. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
104. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
105. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
106. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
107. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
108. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
109. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
110. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
111. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
112. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
113. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
114. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
115. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176

116. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
117. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
118. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
119. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
120. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
121. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
122. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
123. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
124. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
125. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
126. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
127. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
128. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
129. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
130. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
131. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
132. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
133. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
134. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
135. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
136. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
137. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
138. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
139. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
140. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706

141. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
142. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
143. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
144. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
145. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
146. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
147. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
148. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
149. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
150. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
151. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
152. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
153. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
154. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
155. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
156. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
157. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
158. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
159. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
160. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
161. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
162. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
163. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
164. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207

165. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
166. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
167. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
168. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
169. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
170. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
171. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
172. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
173. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
174. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
175. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
176. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
177. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
178. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
179. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
180. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
181. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
182. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
183. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
184. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
185. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
186. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
187. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
188. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
189. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
190. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325

191. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
192. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
193. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
194. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
195. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
196. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
197. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
198. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
199. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
200. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
201. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
202. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
203. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
204. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
205. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
206. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
207. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
208. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
209. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
210. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
211. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
212. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
213. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
214. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1

215. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
216. Daumit GL, Dickerson FB, Wang N-Y, Dalcin A, Jerome GJ, Anderson CAM, et al. A behavioral weight-loss intervention in persons with serious mental illness. N Engl J Med. 2013;368(17):1594-602. doi: 10.1056/NEJMoa1214530
217. Erickson ZD, Mena SJ, Pierre JM, Blum LH, Martin E, Hellemann GS, et al. Behavioral interventions for antipsychotic medication-associated obesity: a randomized, controlled clinical trial. J Clin Psychiatry. 2016;77(2):e183-e9. doi: 10.4088/JCP.14m09552
218. Ma C, Avenell A, Bolland M, Hudson J, Stewart F, Robertson C, et al. Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease, and cancer: systematic review and meta-analysis. BMJ. 2017;359:j4849. doi: 10.1136/bmj.j4849
219. LeBlanc ES, Patnode CD, Webber EM, Redmond N, Rushkin M, O'Connor EA. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2018;320(11):1172-91. doi: 10.1001/jama.2018.7777
220. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
221. Leblanc ES, O'Connor E, Whitlock EP, Patnode CD, Kapka T. Effectiveness of primary care-relevant treatments for obesity in adults: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2011;155(7):434-47. doi: 10.7326/0003-4819-155-7-201110040-00006
222. Dombrowski SU, Avenell A, Sniehott FF. Behavioural interventions for obese adults with additional risk factors for morbidity: systematic review of effects on behaviour, weight and disease risk factors. Obes Facts. 2010;3(6):377-96. doi: 10.1159/000323076
223. Johnson M, Jones R, Freeman C, Woods HB, Gillett M, Goyder E, Payne N. Can diabetes prevention programmes be translated effectively into real-world settings and still deliver improved outcomes? A synthesis of evidence. Diabet Med. 2013;30(1):3-15. doi: 10.1111/dme.12018
224. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
225. Jenum AK, Brekke I, Mdala I, Muilwijk M, Ramachandran A, Kjøllesdal M, et al. Effects of dietary and physical activity interventions on the risk of type 2 diabetes in South Asians: meta-analysis of individual participant data from randomised controlled trials. Diabetologia. 2019;62(8):1337-48. doi: 10.1007/s00125-019-4905-2
226. Kerrison G, Gillis RB, Jiwani SI, Alzahrani Q, Kok S, Harding SE, et al. The effectiveness of lifestyle adaptation for the prevention of prediabetes in adults: a systematic review. J Diabetes Res. 2017;2017:8493145. doi: 10.1155/2017/8493145
227. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. Age Ageing. 2010;39(2):176-84. doi: 10.1093/ageing/afp251
228. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
229. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
230. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
231. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
232. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
233. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
234. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
235. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020

236. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
237. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
238. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
239. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
240. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
241. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
242. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
243. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
244. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
245. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
246. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
247. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
248. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
249. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
250. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
251. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
252. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
253. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
254. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
255. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
256. Halle M, Röhling M, Banzer W, Braumann KM, Kempf K, McCarthy D, et al. Meal replacement by formula diet reduces weight more than a lifestyle intervention alone in patients with overweight or obesity and accompanied cardiovascular risk factors-the ACOORH trial. Eur J Clin Nutr. 2021;75(4):661-9. doi: 10.1038/s41430-020-00783-4
257. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
258. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
259. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347

260. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
261. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227
262. Meenan RT, Stumbo SP, Yarborough MT, Leo MC, Yarborough BJH, Green CA. An economic evaluation of a weight loss intervention program for people with serious mental illnesses taking antipsychotic medications. Adm Policy Ment Health. 2016;43(4):604-15. doi: 10.1007/s10488-015-0669-2

Question: Interventions combining nutrition and physical activity with or without sedentary behaviour compared to treated/untreated comparators for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Nutrition and physical activity interventions* vs untreated comparator (baseline to 12 months)									
2[a]	randomised trials	serious[b]	serious[c]	not serious	serious[d]	none	2/2 studies found a positive effect of combining nutrition and physical activity interventions with or without sedentary behaviour on weight maintenance/loss	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

*No sedentary behaviour interventions were identified in this population, CI: confidence interval

Explanations

a. 2 studies, with 2 intervention arms
b. -1 using RoB-2 risk of bias rated Low (1 (50%) outcome), Some concerns (1 (50% outcome)
c. -1 due to unspecified heterogeneity due to differences in exposure
d. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should interventions combining nutrition, physical activity and psychological vs. treated/untreated comparators be used for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity?	
POPULATION:	People with a mental health condition who were living with overweight or obesity. Studies included in this analysis included participants who had a mental health condition (i.e. schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief reactive psychosis, or psychosis not otherwise specified, bipolar disorder, depressive or anxiety disorder, personality disorder, autism spectrum disorder, other psychiatric disorder) and prescribed an antipsychotic [i.e. olanzapine/clozapine (high weight-gain risk), risperidone/quetiapine (medium weight-gain risk), or aripiprazole/ziprasidone (low weight-gain risk)].
INTERVENTION:	Combined nutrition, physical activity, and psychological interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Mental health conditions increase the propensity for developing obesity (1, 2). People with severe mental illness (e.g., schizophrenia, bipolar disorder affective disorder, major depressive disorder with psychosis) have three times higher odds of obesity than the general population (OR=3.04; 95% CI: 2.42, 3.82) (1). The odds of overweight are equivalent, however (OR=1.07; 95% CI: 0.91, 1.27) (1). Among people with schizophrenia, woman have higher odds of overweight (OR=1.27; 95% CI: 1.16, 1.39) and obesity (OR=1.46; 95% CI: 1.23, 1.72) than men (1). Similarly, people with depression (symptoms and disorder) have higher odds of developing obesity (OR=1.58; 95% CI: 1.33, 1.87) but not overweight (OR=1.20, 95% CI: 0.87, 1.66) (2). Factors contributing to obesity among people with mental health conditions include poor quality diets and eating patterns (3), sedentary behaviour and low physical activity levels (4), and psychotropic medications (5). People with severe mental illness consume more dietary energy (mean difference=1332kJ; 95% CI: 487, 2178) and sodium (mean difference=322mg; 95% CI: 174, 490) than healthy controls (3). The diets of people with severe mental illness tend to be less healthy, with low consumption of fruit and vegetables and high intakes of sugar-sweetened beverages and takeaway and other convenience foods (3). Compared to healthy controls, people with severe mental illness are more sedentary (mean difference=10.1mins/day; 95% CI: 1.9, 22.2) and less engaged in moderate physical activity (mean difference=10.2mins/day; 95% CI: 3.2, 17.2) and vigorous physical activity (mean difference=3.2mins/day; 95%	

	CI: 1.1, 6.4) (4). Weight-gain is a side-effect of nearly all antipsychotic medications, with two second-generation antipsychotics (clozapine and olanzapine) having the greatest potential to produce increases in weight (5). There is a moderate risk of weight gain with other second-generation anti-psychotics (quetiapine, risperidone, paliperidone and iloperidone) (5). The potential for weight gain also exists with first-generation antipsychotics (e.g., chlorpromazine and thioridazine), antidepressants (e.g., amitriptyline, mirtazapine, and paroxetine), and mood stabilizers (lithium, valproate) (5). A number of health risks are associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y). **Children and adolescents (2 to <18y)** <u>Blood pressure indicators</u> Prevalence of prehypertension (6), hypertension and elevated blood pressure (6-11) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (12). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (13, 14). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (6, 9-11). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (12). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (13, 15) and mortality (14, 15) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (14). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (6, 10, 11). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (10, 11). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (13-15).	

Non-alcoholic fatty liver disease
Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (10) and risk of developing non-alcoholic fatty liver disease (6, 16-18) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (19).

Musculoskeletal conditions
Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (20).

Cancer
Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (21), and ovarian (21, 22) cancer during adulthood among women; and colorectal cancer (23) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (24).

Mental health
Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (10) and depression (10, 25) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (26). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (27).

Health-related quality of life ratings
Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (10). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (28).

Reproductive health
Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (29). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (29). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (29).

Young and middle-aged adults (18 to <65y)
Cardiovascular disease

Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (30-41). Cardiovascular disease mortality increased with increasing weight (40, 42-44). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (45, 46), including ischemic stroke (45), and haemorrhagic stroke (45). Risk was also elevated for coronary artery disease (47, 48).

Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (49). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (50).

Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (34, 51-53).

<u>Blood glucose level</u>
A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (54).

<u>Type 2 diabetes mellitus</u>
Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (38, 48, 55-70).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (34, 54, 71-74).

<u>Non-alcoholic fatty liver disease</u>
Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (75-80).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (81-83). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (81).

<u>Musculoskeletal conditions</u>
Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (84). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (85).

<u>Cancer</u>
When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a

range of cancers, including brain (86, 87), thyroid (87-93), and blood cancers such as; lympho-haematopoietic (94) and diffuse large B-cell lymphoma (95, 96), multiple myeloma (87, 96-98), Hodgkin and non-Hodgkin lymphoma (87, 96), and leukemia (99, 100) (obesity only (101)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (70, 86, 87, 92, 98, 99, 102-107), gastroesophageal (108, 109), gastric (87, 92, 107, 110, 111), and stomach (70) cancers; and liver (70, 87, 92, 98, 109, 112-121), gallbladder (70, 87, 98, 99, 122-124), bile duct (125), pancreatic (70, 92, 98, 99, 109, 126-128), small intestinal (126), and colorectal (86, 87, 92, 98, 99, 109, 127, 129-146) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (70, 86, 87, 92, 98, 99, 109, 139, 147-151), and bladder (70, 87, 149, 150, 152-155)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (99) cancers, and total cancer risk was associated with increasing adiposity (156). Increased BMI in adulthood (≥18y) was protective against lung cancer (86, 157, 158), and pre-menopausal breast cancer (86, 159). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (160). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (161).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (87, 109, 162-165) (premenopausal (92, 166, 167) or postmenopausal (139) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (168). Risk of other gynaecological cancers also increased, including endometrial (86, 87, 98, 99, 136, 139, 169-172), uterine (70), and cervical cancers (87) (weak association with obesity (173)), as well as breast cancer (92, 99, 109, 136, 139, 156, 173-185). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (49). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (149, 186, 187), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (86, 188), while risk increased for development of advanced prostate cancer (109, 150, 188, 189) and prostate cancer mortality (190).

Mental health
Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (191). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (192, 193), or depression (194, 195), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (191).

	<u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (196). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (197). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (198). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (199-203). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (204). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (205). **Older adults (≥65y)** <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (206). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (207). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (208). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (208). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (209, 210). <u>Musculoskeletal conditions</u> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (211, 212). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (213, 214). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (215). <u>Cancer</u> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (159).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from meta-analysis</u>: From 2 studies (216, 217) with 175 intervention participants and 142 comparator participants, evidence demonstrated a small effect size of Hedges' g 0.26 lower (95% CI 0.48 lower to 0.04 lower) in the intervention versus comparator. <u>Evidence from narrative synthesis</u>: 2 additional studies (218, 219) unable to be included in the meta-analysis found a positive effect of combining nutrition, physical activity, and psychological interventions for weight maintenance/loss. <u>Additional desirable effects</u>: No evidence was identified in this population the below was derived from young and middle-aged adults. In men only, nutrition, physical activity, and behaviour therapy (e.g., initiatives based on social cognitive theory) interventions (220), showed favourable outcomes for systolic and diastolic blood pressure, plasma glucose, and blood lipids (HDL-C, LDL-C, triglycerides, and total cholesterol). <u>Lived experience:</u> One review paper (221) reported the experiences of people with serious mental illness. Participants reported improved self-esteem and self-efficacy outcomes after nutrition and physical activity programmes that emphasized successes and praised achievements in a non-judgmental and supportive environment (221). Programs tailored to the challenges of mental health conditions (e.g., shorter, repeated sessions with regular breaks, call reminders) supported engagement and attendance (221). The following evidence was taken from studies of young and middle-aged adult populations. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (222-225). Reduction in mental health symptoms including depression and anxiety (226, 227), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (228-232). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (233-237). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (237-240). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (241-244). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (241, 242). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (196, 220, 245, 246). Support for forming exercise habits, accountability, and maintaining motivation	Current available data indicates a reduction in eating disorder symptoms (binge eating) with weight management treatments. Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (247), Healthy China Initiative (248), Finnish Diabetes Prevention Study (249)) overwhelmingly support positive health outcomes of physical activity. In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (250). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (250). Additional benefits may include improved Quality of Life, reduction in depression and anxiety etc.

	facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (245, 246).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analysis</u>: No evidence was identified for this population. <u>Additional undesirable effects</u>: No evidence was identified for this population. <u>Lived experience</u>: One review paper (221) reported the experiences of people with serious mental illness. This group experiences several barriers to behavioural weight management programs. People with mental health conditions reported difficulty initiating and adhering to weight maintenance/loss programs because of fluctuating symptoms and medication side effects, that in turn caused varying motivation, ability, and added stressors to support networks (221). Some medications may affect the ability to manage weight, which may contribute to lower self-esteem. Structural barriers may include prohibitive cost of or inaccessibility of food, gym memberships or equipment, and transport (221). The following evidence was taken from young and middle-aged adult population: Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (220, 235, 241). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (241, 242). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (246). Fears of embarrassment and failure during exercise activities were also reported (220, 239, 246, 251). Cultural and social expectations related to food and alcohol impacted adherence (235, 239) (252). Limited access to culturally appropriate and healthy foods (239), financial constraints (221), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (238, 245, 253-255).	When people who are living with overweight or obesity and a mental illness are participating in a behavioural weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity and a mental illness with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Evidence from meta-analysis: Combining nutrition, physical activity and psychological interventions may reduce adiposity slightly.	

	Evidence from narrative synthesis: The evidence is very uncertain about the effect of this intervention on adiposity.	

Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with a mental health condition and overweight or obesity in relation to receiving combined nutrition, physical activity, and psychological treatment. However, the committee believes that since there are benefits, most people with a mental health condition and overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above, and the committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training.

Resources required How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition, physical activity and psychological interventions are not necessarily widely available and affordable.	Participants reported financial barriers to structured physical activity, included expensive gym memberships, equipment, and clothing. Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Long-term psychological care is often needed, and

		treatment is unlikely to be one-off. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ● Varies ○ No included studies	A 10-week health promotion intervention targeting physical activity and healthy eating in mental health care, when projecting 1-year results over a 20-year time horizon, resulted in a 0.01 gain in quality-adjusted life years (QALYs) (256). From a public payer perspective, the authors estimated the incremental cost-effectiveness ratio (ICER) to be €27,096/QALY in men and €40,139€/QALY in women. Based on a cost-effectiveness threshold of approximately €30,000/QALY in Belgium, the authors concluded that the intervention was cost-effective for men and not women.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Equity is affected by cost of treatments and accessibility of treatments. Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations.

		High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. High cost of psychological care and long wait times may make treatment prohibitive for some people, decreasing health equity. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs; or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no	We have not sourced literature on the acceptability of people living with a mental health condition receiving combined nutrition, physical	Acceptability increases where nutrition, physical

● Probably yes ○ Yes ○ Varies ○ Don't know	activity, and psychological treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people with mental health conditions and overweight or obesity, and clinicians.	activity and psychological treatments are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of people living with a mental health condition receiving combined nutrition, physical activity and psychological interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	**Varies**	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	•	○

CONCLUSIONS

Recommendation

Conditional recommendation for the intervention:

Combined nutrition, physical activity and psychological interventions may be recommended as part of a comprehensive approach for the management of weight-related health and wellbeing.

REFERENCES SUMMARY

1. Afzal M, Siddiqi N, Ahmad B, Afsheen N, Aslam F, Ali A, et al. Prevalence of overweight and obesity in people with severe mental illness: systematic review and meta-analysis. Front Endocrinol. 2021;12. doi: 10.3389/fendo.2021.769309
2. Luppino FS, De Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BWJH, Zitman FG. Overweight, obesity, and depression. Arch Gen Psychiatry. 2010;67(3):220. doi: 10.1001/archgenpsychiatry.2010.2
3. Teasdale SB, Ward PB, Samaras K, Firth J, Stubbs B, Tripodi E, Burrows TL. Dietary intake of people with severe mental illness: systematic review and meta-analysis. Br J Psychiatry. 2019;214(5):251-9. doi: 10.1192/bjp.2019.20
4. Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, et al. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. World Psychiatry. 2017;16(3):308-15. doi: 10.1002/wps.20458
5. Mazereel V, Detraux J, Vancampfort D, Van Winkel R, De Hert M. Impact of psychotropic medication effects on obesity and the metabolic syndrome in people with serious mental illness. Front Endocrinol. 2020;11. doi: 10.3389/fendo.2020.573479
6. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
7. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
8. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
9. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
10. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
11. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
12. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
13. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
14. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
15. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
16. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
17. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
18. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
19. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
20. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
21. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
22. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
23. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3

24. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
25. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
26. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
27. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
28. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
29. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
30. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
31. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
32. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
33. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
34. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
35. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
36. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
37. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
38. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
39. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
40. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
41. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
42. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
43. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
44. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
45. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
46. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304

47. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
48. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
49. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
50. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
51. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
52. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
53. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
54. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
55. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
56. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
57. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
58. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
59. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
60. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
61. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
62. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
63. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
64. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
65. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
66. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
67. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
68. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43

69. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
70. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
71. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
72. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
73. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
74. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
75. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
76. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
77. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
78. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
79. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
80. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
81. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
82. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
83. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
84. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
85. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
86. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
87. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
88. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
89. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
90. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
91. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
92. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
93. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
94. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045

95. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
96. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
97. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
98. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
99. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
100. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
101. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
102. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
103. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
104. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
105. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
106. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
107. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
108. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
109. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
110. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
111. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
112. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
113. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
114. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
115. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
116. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
117. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
118. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
119. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21

120. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
121. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
122. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
123. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
124. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
125. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
126. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
127. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
128. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
129. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
130. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
131. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
132. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
133. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
134. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
135. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
136. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
137. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
138. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
139. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
140. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
141. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
142. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
143. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
144. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434

145. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
146. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
147. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
148. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
149. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
150. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
151. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
152. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
153. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
154. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
155. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
156. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
157. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
158. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
159. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
160. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
161. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
162. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
163. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
164. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
165. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
166. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
167. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
168. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
169. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017

170. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
171. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
172. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
173. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
174. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
175. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
176. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
177. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
178. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
179. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
180. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
181. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
182. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
183. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
184. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
185. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
186. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
187. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
188. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
189. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
190. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
191. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
192. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
193. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
194. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034

195. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
196. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
197. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
198. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
199. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
200. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
201. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
202. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
203. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
204. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
205. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
206. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
207. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
208. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
209. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
210. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
211. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
212. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
213. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
214. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
215. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
216. Lovell K, Wearden A, Bradshaw T, Tomenson B, Pedley R, Davies LM, et al. An exploratory randomized controlled study of a healthy living intervention in early intervention services for psychosis: the INTERvention to encourage ACTivity, improve diet, and reduce weight gain (INTERACT) study. J Clin Psychiatry. 2014;75(5):498-505. doi: 10.4088/JCP.13m08503
217. Walburg FS, van Meijel B, Hoekstra T, Kol J, Pape LM, de Joode JW, et al. Effectiveness of a lifestyle intervention for people with a severe mental illness in dutch outpatient mental health care: a randomized clinical trial. JAMA Psychiatry. 2023;80(9):886-94. doi: 10.1001/jamapsychiatry.2023.1566

218. Erickson ZD, Kwan CL, Gelberg HA, Arnold IY, Chamberlin V, Rosen JA, et al. A randomized, controlled multisite study of behavioral interventions for veterans with mental illness and antipsychotic medication-associated obesity. J Gen Intern Med. 2017;32:32-9. doi: 10.1007/s11606-016-3960-3
219. Green CA, Yarborough BJH, Leo MC, Yarborough MT, Stumbo SP, Janoff SL, et al. The STRIDE weight loss and lifestyle intervention for individuals taking antipsychotic medications: a randomized trial. Am J Psychiatry. 2015;172(1):71-81. doi: 10.1176/appi.ajp.2014.14020173
220. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
221. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
222. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
223. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
224. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
225. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
226. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
227. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
228. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
229. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
230. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
231. Palavras MA, Hay P, Filho CADS, Claudino A. The ffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
232. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
233. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
234. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
235. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
236. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
237. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
238. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
239. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334

240. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
241. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
242. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
243. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
244. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
245. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
246. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
247. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
248. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
249. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
250. Halle M, Röhling M, Banzer W, Braumann KM, Kempf K, McCarthy D, et al. Meal replacement by formula diet reduces weight more than a lifestyle intervention alone in patients with overweight or obesity and accompanied cardiovascular risk factors-the ACOORH trial. Eur J Clin Nutr. 2021;75(4):661-9. doi: 10.1038/s41430-020-00783-4
251. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
252. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
253. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
254. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
255. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227
256. Verhaeghe N, De Smedt D, De Maeseneer J, Maes L, Van Heeringen C, Annemans L. Cost-effectiveness of health promotion targeting physical activity and healthy eating in mental health care. BMC Public Health. 2014;14:856. doi: 10.1186/1471-2458-14-856

Question: Interventions combining nutrition, physical activity and psychological compared to treated/untreated comparators for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	interventions **combining nutrition, physical activity and psychological**	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Nutrition, physical activity, and psychological interventions vs untreated comparator (baseline to 12 months)												
2[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	none	175	142	-	Hedges' g **0.26 lower** (0.48 lower to 0.04 lower)	⨁⨁◯◯ Low	Combined nutrition, physical activity and psychological interventions may reduce adiposity slightly.
Nutrition, physical activity, and psychological interventions vs untreated comparator (baseline to 12 months)												
2[a]	randomised trials	very serious[d]	serious[e]	not serious	serious[c]	none	2/2 studies found a positive effect of combining nutrition, physical activity, and psychological interventions for weight maintenance/loss				⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 2 study, with 2 intervention arms
b. -1 using RoB-2 risk of bias rated Some concerns (3 (75%) outcomes), High (1 (25%) outcome)
c. -1 Imprecision due to small sample size (Total n<400)
d. -2 using RoB-2 risk of bias rated Low (1 (50%) outcome), High (1 (50%) outcome)
e. -1 due to unspecified heterogeneity due to differences in exposure

QUESTION

Should interventions combining nutrition, physical activity and family-centred vs. treated/untreated comparators be used for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity?	
POPULATION:	People with a mental health condition living with overweight or obesity. Studies included in this analysis included participants with dementia.
INTERVENTION:	Combined nutrition, physical activity, and family-centred interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Mental health conditions increase the propensity for developing obesity (1, 2). People with severe mental illness (e.g., schizophrenia, bipolar disorder affective disorder, major depressive disorder with psychosis) have three times higher odds of obesity than the general population (OR=3.04; 95% CI: 2.42, 3.82) (1). The odds of overweight are equivalent, however (OR=1.07; 95% CI: 0.91, 1.27) (1). Among people with schizophrenia, woman have higher odds of overweight (OR=1.27; 95% CI: 1.16, 1.39) and obesity (OR=1.46; 95% CI: 1.23, 1.72) than men (1). Similarly, people with depression (symptoms and disorder) have higher odds of developing obesity (OR=1.58; 95% CI: 1.33, 1.87) but not overweight (OR=1.20, 95% CI: 0.87, 1.66) (2). Factors contributing to obesity among people with mental health conditions include poor quality diets and eating patterns (3), sedentary behaviour and low physical activity levels (4), and psychotropic medications (5). People with severe mental illness consume more dietary energy (mean difference=1332kJ; 95% CI: 487, 2178) and sodium (mean difference=322mg; 95% CI: 174, 490) than healthy controls (3). The diets of people with severe mental illness tend to be less healthy, with low consumption of fruit and vegetables and high intakes of sugar-sweetened beverages and takeaway and other convenience foods (3). Compared to healthy controls, people with severe mental illness are more sedentary (mean difference=10.1mins/day; 95% CI: 1.9, 22.2) and less engaged in moderate physical activity (mean difference=10.2mins/day; 95% CI: 3.2, 17.2) and vigorous physical activity (mean difference=3.2mins/day; 95% CI: 1.1, 6.4) (4). Weight-gain is a side-effect of nearly all antipsychotic medications, with two second-generation antipsychotics (clozapine and olanzapine) having the greatest potential to produce increases in weight (5). There is a moderate risk of weight gain with other second-generation anti-psychotics (quetiapine, risperidone, paliperidone and iloperidone) (5). The potential for weight gain also exists with first-generation antipsychotics (e.g., chlorpromazine and thioridazine), antidepressants (e.g., amitriptyline, mirtazapine, and paroxetine), and mood stabilizers (lithium, valproate) (5).	Antipsychotic medications cause significant weight gain. Weight-gain is greatest with olanzapine followed by asenapine, risperidone, aripiprazole, quetiapine XR, brexpiprazole, cariprazine, and lurasidone.

A number of health risks are associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y).

Children and adolescents (2 to <18y)

<u>Blood pressure indicators</u>

Prevalence of prehypertension (6), hypertension and elevated blood pressure (6-11) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (12). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (13, 14).

<u>Blood lipid profile</u>

Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (6, 9-11). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (12).

<u>Cardiovascular disease</u>

Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (13, 15) and mortality (14, 15) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (14).

<u>Blood glucose level</u>

Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (6, 10, 11). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (10, 11).

<u>Type 2 diabetes mellitus</u>

Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (13-15).

<u>Non-alcoholic fatty liver disease</u>

Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (10) and risk of developing non-alcoholic fatty liver disease (6, 16-18) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (19).

<u>Musculoskeletal conditions</u>

	Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (20). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (21), and ovarian (21, 22) cancer during adulthood among women; and colorectal cancer (23) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (24). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (10) and depression (10, 25) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (26). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (27). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (10). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (28). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (29). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (29). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (29). **Young and middle-aged adults (18 to <65y)** <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (30-41). Cardiovascular disease mortality increased with increasing weight (40, 42-44). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (45, 46), including ischemic stroke (45), and haemorrhagic stroke (45). Risk was also elevated for coronary artery disease (47, 48). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or ‘other’ causes, compared to healthy weight survivors (49). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart	

disease and mortality from cardiovascular disease when compared to healthy weight adults (50).

Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (34, 51-53).

<u>Blood glucose level</u>
A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (54).

<u>Type 2 diabetes mellitus</u>
Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (38, 48, 55-70).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (34, 54, 71-74).

<u>Non-alcoholic fatty liver disease</u>
Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (75-80).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (81-83). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (81).

<u>Musculoskeletal conditions</u>
Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (84). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (85).

<u>Cancer</u>
When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (86, 87), thyroid (87-93), and blood cancers such as; lympho-haematopoietic (94) and diffuse large B-cell lymphoma (95, 96), multiple myeloma (87, 96-98), Hodgkin and non-Hodgkin lymphoma (87, 96), and leukemia (99, 100) (obesity only (101)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (70, 86, 87, 92, 98, 99, 102-107), gastroesophageal (108, 109), gastric (87, 92, 107, 110, 111), and stomach (70) cancers; and liver (70, 87, 92, 98, 109, 112-121), gallbladder (70, 87, 98, 99, 122-124), bile duct (125), pancreatic (70, 92, 98, 99, 109, 126-128), small intestinal (126), and colorectal (86, 87, 92, 98, 99, 109, 127, 129-146) cancers. Overweight or obesity were also associated with greater risk of

	urinary cancers (kidney (70, 86, 87, 92, 98, 99, 109, 139, 147-151), and bladder (70, 87, 149, 150, 152-155)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (99) cancers, and total cancer risk was associated with increasing adiposity (156). Increased BMI in adulthood (≥18y) was protective against lung cancer (86, 157, 158), and pre-menopausal breast cancer (86, 159). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (160). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (161). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (87, 109, 162-165) (premenopausal (92, 166, 167) or postmenopausal (139) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (168). Risk of other gynaecological cancers also increased, including endometrial (86, 87, 98, 99, 136, 139, 169-172), uterine (70), and cervical cancers (87) (weak association with obesity (173)), as well as breast cancer (92, 99, 109, 136, 139, 156, 173-185). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (49). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (149, 186, 187), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (86, 188), while risk increased for development of advanced prostate cancer (109, 150, 188, 189) and prostate cancer mortality (190). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (191). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (192, 193), or depression (194, 195), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (191). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (196). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (197). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (198). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (199-203).	

	Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (204). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (205). **Older adults (≥65y)** Cardiovascular disease The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (206). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (207). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (208). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (208). Type 2 diabetes mellitus Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (209, 210). Musculoskeletal conditions Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (211, 212). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (213, 214). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (215). Cancer A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (159).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from a meta-analysis: No evidence was identified in this population. Additional desirable effects: No evidence was identified in this population. Lived experience: No evidence was identified in this population. The following evidence was taken from young and middle-aged adult population. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (216-219). Reduction in mental health symptoms including depression and anxiety (220, 221), and eating	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (242), Healthy China Initiative (243), Finnish Diabetes Prevention Study (244)) overwhelmingly support positive health outcomes of physical activity. In young and middle-aged adults taking part in weight

	disorder problems including bulimia, binge eating, and emotional eating have been reported (222-226). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (227-231). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (231-234). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (235-238). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (235, 236). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (196, 239-241). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (240, 241).	loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (245). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (245). The benefits of weight loss or maintenance on cardiometabolic outcomes were also considered when making judgement.
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from narrative synthesis: 1 study (246) unable to be included in a meta-analysis found a negative effect for combining nutrition, physical activity, and family-centred interventions on weight maintenance/loss. Weight increased by 0.26 kgs in the intervention arm compared to 0.09 kgs in the comparator arm. Additional undesirable effects: No evidence was identified in this population. Lived experience: The following evidence was taken from young and middle-aged adult population. Adults engaged in behavioural interventions that prescribe nutrition, physical activity and family-centred treatment, who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (229, 235, 239). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (235, 236). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (241). Fears of embarrassment and failure during exercise activities were also reported (233, 239, 241, 247). Cultural and social expectations related to food and alcohol impacted adherence (229, 233) (248). Limited access to culturally appropriate and healthy foods (233), financial constraints (249), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (232, 240, 250-252).	A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity.

Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Combining nutrition, physical activity and family-centred interventions may result in little to no difference in adiposity.	

Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with a mental health condition (dementia) and overweight or obesity in relation to receiving combined nutrition, physical activity, and family-centred treatment. However, the committee believes that since there are benefits, most people with dementia and living with overweight or obesity, and their caregivers would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects Does the balance between desirable and undesirable effects favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ● Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Limited research evidence was identified, demonstrating that people with dementia and living with overweight or obesity who took part in a nutrition, physical activity and family-based intervention gained a trivial amount of weight. The Committee has reached a consensus decision that the balance between the desirable and undesirable effects does not favour the intervention or the comparison.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training. When considering nutrition interventions in older adults living with overweight or obesity, clinicians will need to balance the potential benefit from improving diet quality (and hence improved food and nutrient intakes) versus the need for weight reduction. Healthy dietary approaches with no specific daily energy intake goal may therefore be chosen instead of an energy target diet for

		the above reasons to balance quality of life. Clinical judgement is required for older adults living with overweight or obesity to balance priorities for health care in the presence of co-morbidities (e.g. chronic kidney disease, insulin-requiring diabetes, cancer, etc.) as well as age-related conditions (e.g. sarcopenia, osteoporosis/ osteopenia, etc.) and treatment with medications that have weight or nutrition requirement implications.

Resources required
How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Combined nutrition, physical activity and family-centred interventions are not necessarily widely available and affordable.	Participants reported financial barriers to structured physical activity, included expensive gym memberships, equipment, and clothing. Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Food security and cost of living affect equity. Access to healthy food remains inaccessible and/or unaffordable for disadvantaged or remote populations. High costs of gym memberships, sporting club fees and equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. Local knowledge is important for increasing accessibility to low-cost physical activity options. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

		Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of people living with a mental health condition (dementia) receiving combined nutrition, physical activity, and family-centred treatments. However, the committee believes this intervention is likely to be acceptable to most people with a mental health condition and overweight or obesity, their carers, and clinicians.	Acceptability increases where nutrition, physical activity and family-centred interventions are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of people living with a mental health condition (dementia) receiving combined nutrition, physical activity and family-centred interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	**Does not favour either the intervention or the comparison**	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Combining nutrition, physical activity and family-centred interventions may result in little to no difference in adiposity in people with a mental health condition.

REFERENCES SUMMARY

1. Afzal M, Siddiqi N, Ahmad B, Afsheen N, Aslam F, Ali A, et al. Prevalence of overweight and obesity in people with severe mental illness: systematic review and meta-analysis. Front Endocrinol. 2021;12. doi: 10.3389/fendo.2021.769309
2. Luppino FS, De Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BWJH, Zitman FG. Overweight, obesity, and depression. Arch Gen Psychiatry. 2010;67(3):220. doi: 10.1001/archgenpsychiatry.2010.2
3. Teasdale SB, Ward PB, Samaras K, Firth J, Stubbs B, Tripodi E, Burrows TL. Dietary intake of people with severe mental illness: systematic review and meta-analysis. Br J Psychiatry. 2019;214(5):251-9. doi: 10.1192/bjp.2019.20
4. Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, et al. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. World Psychiatry. 2017;16(3):308-15. doi: 10.1002/wps.20458
5. Mazereel V, Detraux J, Vancampfort D, Van Winkel R, De Hert M. Impact of psychotropic medication effects on obesity and the metabolic syndrome in people with serious mental illness. Front Endocrinol. 2020;11. doi: 10.3389/fendo.2020.573479
6. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
7. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
8. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
9. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
10. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
11. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
12. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
13. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
14. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
15. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
16. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
17. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
18. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
19. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
20. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067

21. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
22. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
23. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
24. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
25. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
26. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
27. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
28. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
29. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
30. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
31. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
32. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
33. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
34. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
35. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
36. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
37. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
38. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
39. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
40. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
41. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
42. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
43. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247

44. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
45. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
46. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
47. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
48. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
49. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
50. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
51. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
52. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
53. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
54. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
55. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
56. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
57. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
58. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
59. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
60. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
61. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
62. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
63. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
64. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
65. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218

66. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
67. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
68. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
69. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
70. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
71. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
72. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
73. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
74. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
75. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
76. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
77. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
78. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
79. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
80. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
81. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
82. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
83. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
84. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
85. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
86. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
87. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
88. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
89. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
90. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
91. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321

92. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
93. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
94. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
95. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
96. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
97. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
98. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
99. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
100. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
101. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
102. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
103. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
104. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
105. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
106. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
107. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
108. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
109. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
110. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
111. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
112. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
113. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
114. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
115. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176

116. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
117. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
118. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
119. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
120. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
121. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
122. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
123. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
124. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
125. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
126. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
127. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
128. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
129. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
130. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
131. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
132. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
133. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
134. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
135. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
136. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
137. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
138. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
139. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
140. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706

141. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
142. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
143. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
144. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
145. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
146. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
147. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
148. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
149. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
150. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
151. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
152. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
153. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
154. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
155. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
156. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
157. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
158. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
159. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
160. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
161. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
162. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
163. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
164. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207

165. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
166. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
167. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
168. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
169. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
170. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
171. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
172. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
173. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
174. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
175. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
176. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
177. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
178. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
179. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
180. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
181. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
182. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
183. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
184. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
185. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
186. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
187. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
188. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
189. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
190. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325

191. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
192. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
193. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
194. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
195. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
196. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
197. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
198. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
199. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
200. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
201. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
202. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
203. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
204. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
205. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
206. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
207. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
208. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
209. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
210. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
211. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
212. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
213. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
214. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1

215. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
216. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
217. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
218. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
219. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
220. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
221. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
222. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
223. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
224. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
225. Palavras MA, Hay P, Filho CADS, Claudino A. The fficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
226. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
227. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
228. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
229. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
230. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
231. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
232. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
233. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
234. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
235. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
236. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500

237. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
238. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
239. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
240. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
241. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
242. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
243. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
244. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
245. Halle M, Röhling M, Banzer W, Braumann KM, Kempf K, McCarthy D, et al. Meal replacement by formula diet reduces weight more than a lifestyle intervention alone in patients with overweight or obesity and accompanied cardiovascular risk factors-the ACOORH trial. Eur J Clin Nutr. 2021;75(4):661-9. doi: 10.1038/s41430-020-00783-4
246. Salva A, Andrieu S, Fernandez E, Schiffrin EJ, Moulin J, Decarli B, et al. Health and nutrition promotion program for patients with dementia (NutriAlz): cluster randomized trial. J Nutr Health Aging. 2011;15(10):822-30. doi: 10.1007/s12603-011-0363-3
247. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
248. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
249. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
250. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
251. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
252. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition, physical activity and family-centred compared to treated/untreated comparators for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Nutrition, physical activity, and family-centred interventions vs untreated comparator (baseline to 12 months)									
1[a]	randomised trials	very serious[b]	not serious	not serious	not serious	none	1/1 study found a negative effect for combining nutrition, physical activity, and family-centred interventions on weight maintenance/loss Weight increased by 0.26 kgs in the intervention arm compared to 0.09 kgs in the comparator arm	⨁⨁◯◯ Low	Combining nutrition, physical activity and family-centred interventions may result in little to no difference in adiposity.

CI: confidence interval

Explanations

a. 1 study, with 1 intervention arm
b. -2 using RoB-2 risk of bias rated High for all outcomes

QUESTION

Should a combination of four or more behavioural interventions vs. treated/untreated comparators be used for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity?	
POPULATION:	People with a mental health condition who were living with overweight or obesity. Studies included in this analysis included participants who had serious mental illness (i.e. schizophrenia, schizoaffective disorder, and first-episode psychosis) and prescribed an antipsychotic [i.e. Haloperidol (oral), Amisulpride (oral), Aripiprazole (oral), Aripiprazole (long-acting injection), Clozapine (oral), Olanzapine (oral), Quetiapine (oral), Risperidone (oral), Risperidone (long-acting injection), Flupentixol (injection), Zuclopenthixol (oral), Zuclopenthixol (long-acting injection), Paliperidone(long-acting injection), or 'other' antipsychotic].
INTERVENTION:	Combination of four or more behavioural interventions vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Mental health conditions increase the propensity for developing obesity (1, 2). People with severe mental illness (e.g., schizophrenia, bipolar disorder affective disorder, major depressive disorder with psychosis) have three times higher odds of obesity than the general population (OR=3.04; 95% CI: 2.42, 3.82) (1). The odds of overweight are equivalent, however (OR=1.07; 95% CI: 0.91, 1.27) (1). Among people with schizophrenia, woman have higher odds of overweight (OR=1.27; 95% CI: 1.16, 1.39) and obesity (OR=1.46; 95% CI: 1.23, 1.72) than men (1). Similarly, people with depression (symptoms and disorder) have higher odds of developing obesity (OR=1.58; 95% CI: 1.33, 1.87) but not overweight (OR=1.20, 95% CI: 0.87, 1.66) (2). Factors contributing to obesity among people with mental health conditions include poor quality diets and eating patterns (3), sedentary behaviour and low physical activity levels (4), and psychotropic medications (5). People with severe mental illness consume more dietary energy (mean difference=1332kJ; 95% CI: 487, 2178) and sodium (mean difference=322mg; 95% CI: 174, 490) than healthy controls (3). The diets of people with severe mental illness tend to be less healthy, with low consumption of fruit and vegetables and high intakes of sugar-sweetened beverages and takeaway and other convenience foods (3). Compared to healthy controls, people with severe mental illness are more sedentary (mean difference=10.1mins/day; 95% CI: 1.9, 22.2) and less engaged in moderate physical activity (mean difference=10.2mins/day; 95% CI: 3.2, 17.2) and vigorous physical activity (mean difference=3.2mins/day; 95% CI: 1.1, 6.4) (4). Weight-gain is a side-effect of nearly all antipsychotic medications, with two second-generation antipsychotics (clozapine and olanzapine) having the greatest potential to produce increases in weight	Antipsychotic medications cause significant weight gain. Weight-gain is greatest with olanzapine followed by asenapine, risperidone, aripiprazole, quetiapine XR, brexpiprazole, cariprazine, and lurasidone.

	(5). There is a moderate risk of weight gain with other second-generation anti-psychotics (quetiapine, risperidone, paliperidone and iloperidone) (5). The potential for weight gain also exists with first-generation antipsychotics (e.g., chlorpromazine and thioridazine), antidepressants (e.g., amitriptyline, mirtazapine, and paroxetine), and mood stabilizers (lithium, valproate) (5). A number of health risks are associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y). **Children and adolescents (2 to <18y)** Blood pressure indicators Prevalence of prehypertension (6), hypertension and elevated blood pressure (6-11) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (12). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (13, 14). Blood lipid profile Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (6, 9-11). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (12). Cardiovascular disease Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (13, 15) and mortality (14, 15) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (14). Blood glucose level Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (6, 10, 11). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (10, 11). Type 2 diabetes mellitus Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (13-15). Non-alcoholic fatty liver disease Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (10) and risk of developing non-alcoholic fatty liver disease (6, 16-18) were prevalent among children and adolescents living with overweight or obesity. A systematic review	

	examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (19). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (20). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (21), and ovarian (21, 22) cancer during adulthood among women; and colorectal cancer (23) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (24). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (10) and depression (10, 25) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (26). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (27). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (10). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (28). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (29). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (29). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (29). **Young and middle-aged adults (18 to <65y)** <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (30-41). Cardiovascular disease mortality increased with increasing weight (40, 42-44). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk	

of stroke (45, 46), including ischemic stroke (45), and haemorrhagic stroke (45). Risk was also elevated for coronary artery disease (47, 48).

Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or ‘other’ causes, compared to healthy weight survivors (49). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (50).

Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants’ risk of mortality from cardiovascular disease decreased (34, 51-53).

<u>Blood glucose level</u>
A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (54).

<u>Type 2 diabetes mellitus</u>
Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (38, 48, 55-70).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (34, 54, 71-74).

<u>Non-alcoholic fatty liver disease</u>
Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (75-80).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (81-83). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (81).

<u>Musculoskeletal conditions</u>
Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (84). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (85).

<u>Cancer</u>
When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (86, 87), thyroid (87-93), and blood cancers such as; lympho-haematopoietic (94) and diffuse large B-cell lymphoma (95, 96), multiple myeloma (87, 96-98), Hodgkin and non-Hodgkin lymphoma (87, 96), and leukemia (99, 100) (obesity only (101)).

	Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (70, 86, 87, 92, 98, 99, 102-107), gastroesophageal (108, 109), gastric (87, 92, 107, 110, 111), and stomach (70) cancers; and liver (70, 87, 92, 98, 109, 112-121), gallbladder (70, 87, 98, 99, 122-124), bile duct (125), pancreatic (70, 92, 98, 99, 109, 126-128), small intestinal (126), and colorectal (86, 87, 92, 98, 99, 109, 127, 129-146) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (70, 86, 87, 92, 98, 99, 109, 139, 147-151), and bladder (70, 87, 149, 150, 152-155)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (99) cancers, and total cancer risk was associated with increasing adiposity (156). Increased BMI in adulthood (≥18y) was protective against lung cancer (86, 157, 158), and pre-menopausal breast cancer (86, 159). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (160). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (161). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (87, 109, 162-165) (premenopausal (92, 166, 167) or postmenopausal (139) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (168). Risk of other gynaecological cancers also increased, including endometrial (86, 87, 98, 99, 136, 139, 169-172), uterine (70), and cervical cancers (87) (weak association with obesity (173)), as well as breast cancer (92, 99, 109, 136, 139, 156, 173-185). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (49). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (149, 186, 187), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (86, 188), while risk increased for development of advanced prostate cancer (109, 150, 188, 189) and prostate cancer mortality (190). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (191). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (192, 193), or depression (194, 195), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (191). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (196). <u>Reproductive health</u>	

<table>
<tr><td></td><td>Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (197). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (198). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (199-203).

Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (204). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (205).

Older adults (≥65y)
<u>Cardiovascular disease</u>
The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (206). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (207).
Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (208). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (208).

<u>Type 2 diabetes mellitus</u>
Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (209, 210).

<u>Musculoskeletal conditions</u>
Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (211, 212). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (213, 214). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (215).

<u>Cancer</u>
A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (159).</td><td></td></tr>
<tr><td colspan="3">Desirable Effects
How substantial are the desirable anticipated effects?</td></tr>
<tr><td>JUDGEMENT</td><td>RESEARCH EVIDENCE</td><td>ADDITIONAL CONSIDERATIONS</td></tr>
<tr><td>● Trivial
○ Small
○ Moderate
○ Large
○ Varies</td><td><u>Evidence from narrative synthesis</u>:
1 study (216) unable to be included in a meta-analysis found no effect of combining four or more interventions on weight maintenance/loss. Both intervention and comparator arms lost 0.5% of their body weight at 12 months.</td><td>Less is known about the effects of multimodal approaches to weight management, due in part to study heterogeneity and low</td></tr>
</table>

○ Don't know	 Additional desirable effects: No evidence was identified in this population. Lived experience: One review paper (217) reported the experiences of people with serious mental illness. Participants reported improved self-esteem and self-efficacy outcomes after nutrition and physical activity programmes that emphasized successes and praised achievements in a non-judgmental and supportive environment (217). Programs tailored to the challenges of mental health conditions (e.g., shorter, repeated sessions with regular breaks, call reminders) supported engagement and attendance (217). The following evidence was taken from studies of young and middle-aged adult populations. Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (218-221). Reduction in mental health symptoms including depression and anxiety (222, 223), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (224-228). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (229-233). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (233-236). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (237-240). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (237, 238). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (196, 241-243). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (242, 243).	availability of evidence. However, some patients may be encouraged to take up multimodal treatments with specific tailoring to their needs. Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (244), Healthy China Initiative (245), Finnish Diabetes Prevention Study (246)) overwhelmingly support positive health outcomes of physical activity.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from meta-analysis: No evidence was identified in this population. Additional undesirable effects: No evidence was identified in this population. Lived experience: One review paper (217) reported the experiences of people with serious mental illness. This group experiences several barriers to behavioural weight management programs. People with mental health conditions reported difficulty initiating and adhering to weight maintenance/loss programs because of fluctuating symptoms and medication side effects, that in turn caused varying motivation, ability, and added stressors to support networks (217). Some medications may affect the ability to manage weight, which may contribute to lower self-esteem. Structural	When people who are living with overweight or obesity are participating in a behavioural weight loss intervention that incorporates diet change, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. A low but real risk of incidental musculoskeletal injury exists for people with

	barriers may include prohibitive cost of or inaccessibility of food, gym memberships or equipment, and transport (217). The following evidence was taken from young and middle-aged adult population: Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (231, 237, 241). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (237, 238). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (243). Fears of embarrassment and failure during exercise activities were also reported (235, 241, 243, 247). Cultural and social expectations related to food and alcohol impacted adherence (231, 235) (248). Limited access to culturally appropriate and healthy foods (235), financial constraints (217), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (234, 242, 249-251).	overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity and a mental illness, with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. A combination of four or more behavioural interventions likely results in little to no difference in adiposity.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with a mental health condition and overweight or obesity in relation to receiving a combination of four or more behavioural interventions.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.
Balance of effects Does the balance between desirable and undesirable effects favours the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the	Limited research evidence was identified, however, given the effectiveness of multimodal interventions for the adult population. The Committee has reached a consensus decision that the balance between the desirable and	While some people living with overweight or obesity may experience loss of lean

comparison ○ Does not favours either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● Don't know	undesirable effects is unknown.	mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. A combination of four or more behavioural interventions are not necessarily widely available and affordable.	Dietitians are expensive via the private system, and patients may experience a lack of access through the public health system. Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. Long-term psychological care is often needed, and treatment is unlikely to be one-off. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favours the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favours either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	Equity is affected by cost of treatments and accessibility of treatments. Food security and cost of living affect equity. Healthy food remains inaccessible and unaffordable for disadvantaged or remote populations. High costs of gym memberships, club fees and equipment are borne by participants, and may be prohibitive for some people, decreasing health equity. High cost of psychological care and long wait times may make treatment prohibitive for some people, decreasing health equity. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost physical activity programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e.,

		gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of people living with a mental health condition receiving a combination of four or more behavioural treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people experiencing serious mental illness with overweight or obesity, and clinicians.	Acceptability increases where multiple interventions (including nutrition, physical activity, sedentary behaviour, and psychological treatments) are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of a people living with a mental health condition receiving combination of four or more behavioural interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favours either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**Don't know**
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favours either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

A combination of four or more behavioural interventions likely results in little to no difference in adiposity.

REFERENCES SUMMARY

1. Afzal M, Siddiqi N, Ahmad B, Afsheen N, Aslam F, Ali A, et al. Prevalence of overweight and obesity in people with severe mental illness: systematic review and meta-analysis. Front Endocrinol. 2021;12. doi: 10.3389/fendo.2021.769309
2. Luppino FS, De Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BWJH, Zitman FG. Overweight, obesity, and depression. Arch Gen Psychiatry. 2010;67(3):220. doi: 10.1001/archgenpsychiatry.2010.2
3. Teasdale SB, Ward PB, Samaras K, Firth J, Stubbs B, Tripodi E, Burrows TL. Dietary intake of people with severe mental illness: systematic review and meta-analysis. Br J Psychiatry. 2019;214(5):251-9. doi: 10.1192/bjp.2019.20
4. Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, et al. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. World Psychiatry. 2017;16(3):308-15. doi: 10.1002/wps.20458
5. Mazereel V, Detraux J, Vancampfort D, Van Winkel R, De Hert M. Impact of psychotropic medication effects on obesity and the metabolic syndrome in people with serious mental illness. Front Endocrinol. 2020;11. doi: 10.3389/fendo.2020.573479
6. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
7. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
8. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
9. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
10. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
11. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
12. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
13. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
14. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
15. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
16. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
17. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
18. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
19. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
20. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067

21. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
22. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
23. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
24. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
25. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
26. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
27. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
28. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
29. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
30. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
31. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
32. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
33. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
34. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
35. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
36. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
37. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
38. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
39. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
40. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
41. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
42. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
43. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247

44. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
45. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
46. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
47. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
48. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
49. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
50. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
51. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
52. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
53. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
54. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
55. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
56. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
57. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
58. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
59. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
60. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
61. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
62. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
63. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
64. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
65. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218

66. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
67. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
68. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
69. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
70. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
71. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
72. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
73. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
74. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
75. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
76. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
77. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
78. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
79. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
80. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
81. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
82. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
83. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
84. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
85. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
86. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
87. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
88. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
89. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
90. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
91. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321

92. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
93. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
94. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
95. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
96. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
97. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
98. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
99. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
100. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
101. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
102. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
103. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
104. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
105. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
106. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
107. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
108. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
109. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
110. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
111. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
112. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
113. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
114. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
115. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176

116. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
117. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
118. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
119. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
120. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
121. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
122. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
123. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
124. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
125. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
126. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
127. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
128. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
129. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
130. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
131. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
132. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
133. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
134. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
135. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
136. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
137. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
138. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
139. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
140. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706

141. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
142. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
143. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
144. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
145. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
146. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
147. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
148. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
149. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
150. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
151. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
152. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
153. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
154. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
155. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
156. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
157. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
158. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
159. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
160. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
161. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
162. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
163. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
164. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207

165. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
166. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
167. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
168. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
169. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
170. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
171. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
172. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
173. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
174. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
175. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
176. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
177. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
178. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
179. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
180. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
181. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
182. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
183. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
184. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
185. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
186. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
187. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
188. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
189. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
190. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325

191. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
192. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
193. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
194. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
195. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
196. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
197. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
198. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
199. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
200. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
201. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
202. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
203. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
204. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
205. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
206. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
207. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
208. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
209. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
210. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
211. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
212. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
213. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
214. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1

215. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
216. Holt RIG, Gossage-Worrall R, Hind D, Bradburn MJ, McCrone P, Morris T, et al. Structured lifestyle education for people with schizophrenia, schizoaffective disorder and first-episode psychosis (STEPWISE): randomised controlled trial. Br J Psychiatry. 2019;214(2):63-73. doi: 10.1192/bjp.2018.167
217. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
218. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
219. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
220. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
221. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
222. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
223. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
224. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
225. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
226. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
227. Palavras MA, Hay P, Filho CADS, Claudino A. The fficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
228. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
229. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
230. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
231. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
232. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
233. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
234. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
235. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
236. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481

237. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
238. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
239. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
240. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
241. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
242. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
243. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
244. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
245. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
246. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
247. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
248. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
249. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
250. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
251. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: A combination of four or more behavioural interventions compared to treated/untreated comparators for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
A combination of four or more behavioural interventions vs untreated comparator (baseline to 12 months)									
1[a]	randomised trials	not serious	not serious	not serious	serious[b]	none	1/1 study found no effect of combining four or more interventions on weight maintenance/loss Both intervention and comparator arms lost 0.5% of their body weight at 12 months	⨁⨁⨁◯ Moderate	A combination of four or more interventions likely results in little to no difference in adiposity.

CI: confidence interval

Explanations

a. 1 study, with 1 intervention arm
b. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should pharmacological interventions vs. treated/untreated comparators be used for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity?	
POPULATION:	People with a mental health condition who were living with overweight or obesity. Studies included in this analysis included participants who had serious mental illness (i.e. schizophrenia-spectrum disorder) and prescribed an antipsychotic [i.e. Clozapine (oral), or Olanzapine (oral)].
INTERVENTION:	Pharmacological interventions: **Pharmacological interventions approved for the treatment of overweight or obesity** N/A **Pharmacological interventions prescribed for health outcomes other than obesity that result in weight loss**: • Glucagon-like peptide-1 receptor agonists drug class (Liraglutide, 1.8mg per day) interventions vs any comparator (baseline to final end-point)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Guideline Development Committee members with potential Conflicts of Interest as detailed in 'Management of competing interests' section of the Guideline document participated in discussions but were not part of final recommendation development.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Mental health conditions increase the propensity for developing obesity (1, 2). People with severe mental illness (e.g., schizophrenia, bipolar disorder affective disorder, major depressive disorder with psychosis) have three times higher odds of obesity than the general population (OR=3.04; 95% CI: 2.42, 3.82) (1). The odds of overweight are equivalent, however (OR=1.07; 95% CI: 0.91, 1.27) (1). Among people with schizophrenia, woman have higher odds of overweight (OR=1.27; 95% CI: 1.16, 1.39) and obesity (OR=1.46; 95% CI: 1.23, 1.72) than men (1). Similarly, people with depression (symptoms and disorder) have higher odds of developing obesity (OR=1.58; 95% CI: 1.33, 1.87) but not overweight (OR=1.20, 95% CI: 0.87, 1.66) (2). Factors contributing to obesity among people with mental health conditions include poor quality diets and eating patterns (3), sedentary behaviour and low physical activity levels (4), and psychotropic medications (5). People with severe mental illness consume more dietary energy (mean difference=1332kJ; 95% CI: 487, 2178) and sodium (mean difference=322mg; 95% CI: 174, 490) than healthy controls (3). The diets of people with severe mental illness tend to be less healthy, with low consumption of fruit and vegetables and high intakes of sugar-sweetened beverages and takeaway and other convenience foods (3). Compared to healthy controls, people with severe mental illness are more sedentary (mean difference=10.1mins/day; 95% CI: 1.9, 22.2) and less engaged in moderate physical activity (mean difference=10.2mins/day; 95% CI: 3.2, 17.2) and vigorous physical activity (mean difference=3.2mins/day; 95%	Antipsychotic medications cause significant weight gain. Weight-gain is greatest by olanzapine followed with asenapine, risperidone, aripiprazole, quetiapine XR, brexpiprazole, cariprazine, and lurasidone.

CI: 1.1, 6.4) (4). Weight-gain is a side-effect of nearly all antipsychotic medications, with two second-generation antipsychotics (clozapine and olanzapine) having the greatest potential to produce increases in weight (5). There is a moderate risk of weight gain with other second-generation anti-psychotics (quetiapine, risperidone, paliperidone and iloperidone) (5). The potential for weight gain also exists with first-generation antipsychotics (e.g., chlorpromazine and thioridazine), antidepressants (e.g., amitriptyline, mirtazapine, and paroxetine), and mood stabilizers (lithium, valproate) (5).
A number of health risks are associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y).

Children and adolescents (2 to <18y)
Blood pressure indicators
Prevalence of prehypertension (6), hypertension and elevated blood pressure (6-11) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (12). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (13, 14).

Blood lipid profile
Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (6, 9-11). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (12).

Cardiovascular disease
Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (13, 15) and mortality (14, 15) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (14).

Blood glucose level
Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (6, 10, 11). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (10, 11).

Type 2 diabetes mellitus
Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (13-15).

Non-alcoholic fatty liver disease

	Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (10) and risk of developing non-alcoholic fatty liver disease (6, 16-18) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (19). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (20). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (21), and ovarian (21, 22) cancer during adulthood among women; and colorectal cancer (23) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (24). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (10) and depression (10, 25) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (26). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (27). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (10). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (28). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (29). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (29). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (29). **Young and middle-aged adults (18 to <65y)** <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (30-41). Cardiovascular disease mortality increased with increasing	

	weight (40, 42-44). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (45, 46), including ischemic stroke (45), and haemorrhagic stroke (45). Risk was also elevated for coronary artery disease (47, 48). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (49). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (50). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (34, 51-53). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (54). <u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (38, 48, 55-70). Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (34, 54, 71-74). <u>Non-alcoholic fatty liver disease</u> Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (75-80). Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (81-83). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (81). <u>Musculoskeletal conditions</u> Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (84). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (85). <u>Cancer</u> When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (86, 87), thyroid (87-93), and blood cancers such as; lympho-haematopoietic (94) and diffuse large B-cell lymphoma (95, 96), multiple myeloma (87, 96-98), Hodgkin and non-Hodgkin lymphoma (87, 96), and leukemia (99, 100) (obesity only (101)).	

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (70, 86, 87, 92, 98, 99, 102-107), gastroesophageal (108, 109), gastric (87, 92, 107, 110, 111), and stomach (70) cancers; and liver (70, 87, 92, 98, 109, 112-121), gallbladder (70, 87, 98, 99, 122-124), bile duct (125), pancreatic (70, 92, 98, 99, 109, 126-128), small intestinal (126), and colorectal (86, 87, 92, 98, 99, 109, 127, 129-146) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (70, 86, 87, 92, 98, 99, 109, 139, 147-151), and bladder (70, 87, 149, 150, 152-155)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (99) cancers, and total cancer risk was associated with increasing adiposity (156). Increased BMI in adulthood (≥18y) was protective against lung cancer (86, 157, 158), and pre-menopausal breast cancer (86, 159). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (160). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (161).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (87, 109, 162-165) (premenopausal (92, 166, 167) or postmenopausal (139) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (168). Risk of other gynaecological cancers also increased, including endometrial (86, 87, 98, 99, 136, 139, 169-172), uterine (70), and cervical cancers (87) (weak association with obesity (173)), as well as breast cancer (92, 99, 109, 136, 139, 156, 173-185). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (49). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (149, 186, 187), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (86, 188), while risk increased for development of advanced prostate cancer (109, 150, 188, 189) and prostate cancer mortality (190).

<u>Mental health</u>
Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (191). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (192, 193), or depression (194, 195), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (191).

<u>Health-related quality of life ratings</u>
Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (196).

<u>Reproductive health</u>

	Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (197). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (198). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (199-203). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (204). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (205). **Older adults (≥65y)** <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (206). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (207). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (208). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (208). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (209, 210). <u>Musculoskeletal conditions</u> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (211, 212). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (213, 214). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (215). <u>Cancer</u> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (159).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies	<u>Evidence from narrative synthesis:</u> 1 study (216) unable to be included in a meta-analysis found a positive effect of glucagon-like peptide-1 receptor agonists (Liraglutide 1.8mg) on weight maintenance/loss. Weight reduced by 2.4 kgs in the intervention group compared to a gain of 0.1 kgs in the comparator arm.	Clinicians should be aware that each drug class has a different profile of additional benefits which may be relevant when prescribing.

● Don't know	Additional desirable effects: No evidence was identified in this population the below evidence was drawn from the young and middle-aged population. Specific medications had reported beneficial outcomes for type 2 diabetes (lipase inhibitors (217), anorectic and anticonvulsants (217), GLP-1 [semaglutide] (217), and biguanide (72, 218), cardiovascular mortality (opioid antagonist plus norepinephrine-dopamine reuptake inhibitor (217)), global HRQoL (opioid antagonist plus norepinephrine-dopamine reuptake inhibitor (217)) and physical function (GLP-1 [semaglutide] (219)), systolic blood pressure (anorectic and anticonvulsants (217), GLP-1 [semaglutide and liraglutide] (217), and biguanide (218)), diastolic blood pressure (lipase inhibitors (217), anorectic and anticonvulsants (217), and GLP-1 [semaglutide and liraglutide] (217)), fasting glucose (lipase inhibitors (220) and biguanide (218)), HDL-C (lipase inhibitors (217), anorectic and anticonvulsants (217), GLP-1 [semaglutide and liraglutide] (217), and opioid antagonist plus norepinephrine-dopamine reuptake inhibitor (217)), LDL-C (lipase inhibitors (217)), and total cholesterol (lipase inhibitors (217)). For young and middle-aged adults with type 2 diabetes participating in pharmacological weight management/loss interventions, specific medications had favourable outcomes for systolic and diastolic blood pressure (GLP-1 receptor agonists [semaglutide] (221)), fasting plasma glucose levels (lipase inhibitors (222)), and HbA1c (lipase inhibitors (217) and GLP-1 receptor agonists [semaglutide and liraglutide] (217)). Reported favourable outcomes for young and middle-aged adults without type 2 diabetes participating in pharmacological weight management/loss interventions involving GLP-1 receptor agonists (liraglutide, semaglutide) were reduced systolic and diastolic blood pressure, reduced fasting blood glucose, increased HDL-C, and reduced LDL-C and triglycerides (223). Lived experience: No evidence was identified in this population. The following evidence was taken from young and middle-aged adult population. Studies of adults engaged in pharmacological interventions showed increases in health-related quality of life, physical functioning, and mental functioning (224-226).	Weight loss is typically lower in people living with diabetes compared to those without diabetes, however health benefits are still experienced. Studies of other medications approved for weight management (phentermine) and those commonly used off-label (e.g. topiramate) did not qualify for inclusion in this review. Additional studies demonstrated cardiovascular benefits, including reduction in CV mortality, however these studies did not meet inclusion criteria of this review.
Undesirable Effects How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from meta-analysis: No evidence was identified in this population. Additional undesirable effects: No evidence was identified in this population the below evidence was drawn from the young and middle-aged population. Adverse outcomes reported in reviews of pharmacological interventions were increased systolic and diastolic blood pressure with opioid antagonist plus norepinephrine-dopamine reuptake inhibitor (217), and adverse events with various medications (217-220).	Clinicians should be aware each drug class has a different profile of adverse effects, which may be relevant when prescribing. Medication-related adverse effects are common, most are mild and often transient. Many adverse effects can be minimised or mitigated by starting at a low dose

	Specifically in adults without type 2 diabetes, adverse outcomes with GLP-1 receptor agonists (liraglutide, semaglutide) were increased nausea, vomiting, diarrhoea, constipation, abdominal pain, dyspepsia, hypoglycaemia, and neoplasms (223). <u>Lived experience:</u> No evidence was identified in this population.	followed by a gradual increase. Regular review of medication and long-term follow-up are necessary. Awareness of possible drug-drug interactions is necessary. These differ by drug class. There is very limited long-term data from pharmacological studies. Evidence is rapidly evolving - need for regular revision. In addition to intentional adiposity loss, some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss.
Certainty of evidence What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Pharmacological intervention likely reduces adiposity.	
Values Is there important uncertainty about or variability in how much people value the main outcomes?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of people living with overweight or obesity in relation to receiving pharmacological interventions. However, the committee believes that since there are benefits, most people with a mental health condition and overweight or obesity would opt for this treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management. A lack of availability for people who meet treatment guidelines has highlighted the widespread demand/unmet need for pharmacological interventions.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favors the intervention ○ Varies ○ Don't know	Limited research evidence was identified, however, given the effectiveness of pharmacological interventions for the adult population, the Committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Pharmacological interventions are not necessarily widely available and affordable.	Currently there is no subsidisation of pharmacological interventions by the PBS, and the entire treatment cost is covered by patients. Off-label use of topiramate is common because of cost and availability of alternative weight management medications. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison ● Probably favours the intervention o Favors the intervention o Varies o No included studies	In a cost-effectiveness analysis in a US setting (227), the QALYs gained (presumably over a week) were 0.0032 years for liraglutide (1.8mg daily, subcutaneous). The change in QALYs with no treatment was -0.0002.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased ● Varies o Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	While widely available and accessible pharmacological interventions increase health equity, large barriers to accessibility of pharmacological interventions exist for many people. The need to self-fund treatment decreases equity. Current drug costs and reimbursement structures of medications are a barrier to equity. When discussing the patient's care plan, practitioners should take into consideration whether the patient may face out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these

		populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising the patient's awareness of locally available adjunct treatments and avenues for access. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving pharmacological interventions. However, the committee believes this intervention is likely to be acceptable to the majority of people with overweight or obesity, and clinicians.	Stigma may reduce acceptability of this treatment to patients and clinicians. Some patients or clinicians may not deem pharmacological interventions for weight management in adults to be acceptable. Acceptability increases where adjunct treatments are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of pharmacological interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Medication shortages and supply issues may decrease feasibility of pharmacological interventions. Current pharmacological intervention costs and reimbursement

		structures of medications are a barrier to feasibility. Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favors the intervention	Varies	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Pharmacological interventions approved for weight management may be considered as part of as part of a comprehensive treatment program to improve weight-related health and wellbeing.

REFERENCES SUMMARY

1. Afzal M, Siddiqi N, Ahmad B, Afsheen N, Aslam F, Ali A, et al. Prevalence of overweight and obesity in people with severe mental illness: systematic review and meta-analysis. Front Endocrinol. 2021;12. doi: 10.3389/fendo.2021.769309
2. Luppino FS, De Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BWJH, Zitman FG. Overweight, obesity, and depression. Arch Gen Psychiatry. 2010;67(3):220. doi: 10.1001/archgenpsychiatry.2010.2
3. Teasdale SB, Ward PB, Samaras K, Firth J, Stubbs B, Tripodi E, Burrows TL. Dietary intake of people with severe mental illness: systematic review and meta-analysis. Br J Psychiatry. 2019;214(5):251-9. doi: 10.1192/bjp.2019.20
4. Vancampfort D, Firth J, Schuch FB, Rosenbaum S, Mugisha J, Hallgren M, et al. Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. World Psychiatry. 2017;16(3):308-15. doi: 10.1002/wps.20458
5. Mazereel V, Detraux J, Vancampfort D, Van Winkel R, De Hert M. Impact of psychotropic medication effects on obesity and the metabolic syndrome in people with serious mental illness. Front Endocrinol. 2020;11. doi: 10.3389/fendo.2020.573479
6. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
7. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
8. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
9. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
10. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
11. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
12. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
13. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
14. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
15. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
16. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
17. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
18. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
19. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
20. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067

21. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
22. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
23. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
24. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
25. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
26. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
27. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
28. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
29. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
30. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
31. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
32. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
33. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
34. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
35. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
36. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
37. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
38. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
39. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
40. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
41. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
42. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
43. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247

44. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
45. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
46. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
47. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
48. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
49. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
50. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
51. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
52. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
53. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
54. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
55. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
56. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
57. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
58. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
59. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
60. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
61. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
62. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
63. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
64. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
65. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218

66. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
67. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
68. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
69. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
70. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
71. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
72. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
73. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
74. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
75. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
76. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
77. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
78. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
79. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
80. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
81. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
82. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
83. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
84. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
85. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
86. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
87. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
88. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
89. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
90. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
91. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321

92. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
93. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
94. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
95. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
96. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
97. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
98. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
99. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
100. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
101. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
102. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
103. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
104. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
105. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
106. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
107. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
108. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
109. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
110. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
111. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
112. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
113. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
114. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
115. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176

116. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
117. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
118. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
119. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
120. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
121. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
122. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
123. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
124. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
125. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
126. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
127. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
128. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
129. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
130. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
131. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
132. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
133. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
134. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
135. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
136. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
137. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
138. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
139. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
140. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706

141. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
142. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
143. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
144. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
145. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
146. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
147. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
148. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
149. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
150. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
151. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
152. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
153. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
154. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
155. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
156. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
157. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
158. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
159. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
160. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
161. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
162. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
163. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
164. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207

165. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
166. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
167. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
168. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
169. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
170. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
171. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
172. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
173. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
174. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
175. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
176. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
177. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
178. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
179. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
180. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
181. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
182. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
183. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
184. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
185. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
186. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
187. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
188. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
189. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
190. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325

191. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
192. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
193. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
194. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
195. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
196. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
197. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
198. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
199. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
200. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
201. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
202. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
203. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
204. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
205. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
206. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
207. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
208. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
209. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
210. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
211. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
212. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
213. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
214. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1

215. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
216. Svensson CK, Larsen JR, Vedtofte L, Jakobsen MSL, Jespersen HR, Jakobsen MI, et al. One-year follow-up on liraglutide treatment for prediabetes and overweight/obesity in clozapine- or olanzapine-treated patients. Acta Psychiatr Scand. 2019;139(1):26-36. doi: 10.1111/acps.12982
217. Iannone A, Natale P, Palmer SC, Nicolucci A, Rendina M, Giorgino F, et al. Clinical outcomes associated with drugs for obesity and overweight: a systematic review and network meta-analysis of randomized controlled trials. Diabetes Obes Metab. 2023;25(9):2535-44. doi: 10.1111/dom.15138
218. Leblanc ES, O'Connor E, Whitlock EP, Patnode CD, Kapka T. Effectiveness of primary care-relevant treatments for obesity in adults: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2011;155(7):434-47. doi: 10.7326/0003-4819-155-7-201110040-00006
219. He K, Guo Q, Zhang H, Xi W, Li J, Jing Z. Once-weekly semaglutide for obesity or overweight: a systematic review and meta-analysis. Diabetes Obes Metab. 2022;24(4):722-6. doi: 10.1111/dom.14612
220. Zhou Y-H, Ma X-Q, Wu C, Lu J, Zhang S-S, Guo J, et al. Effect of anti-obesity drug on cardiovascular risk factors: a systematic review and meta-analysis of randomized controlled trials. PLoS ONE. 2012;7(6):e39062. doi: 10.1371/journal.pone.0039062
221. Tsapas A, Karagiannis T, Kakotrichi P, Avgerinos I, Mantsiou C, Tousinas G, et al. Comparative efficacy of glucose-lowering medications on body weight and blood pressure in patients with type 2 diabetes: a systematic review and network meta-analysis. Diabetes Obes Metab. 2021;23(9):2116-24. doi: 10.1111/dom.14451
222. Aldekhail NM, Logue J, McLoone P, Morrison DS. Effect of orlistat on glycaemic control in overweight and obese patients with type 2 diabetes mellitus: a systematic review and meta-analysis of randomized controlled trials. Obes Rev. 2015;16(12):1071-80. doi: 10.1111/obr.12318
223. Iqbal J, Wu H-X, Hu N, Zhou Y-H, Li L, Xiao F, et al. Effect of glucagon-like peptide-1 receptor agonists on body weight in adults with obesity without diabetes mellitus-a systematic review and meta-analysis of randomized control trials. Obes Rev. 2022;23(6):e13435. doi: 10.1111/obr.13435
224. Fabricatore AN, Wadden TA, Higginbotham AJ, Faulconbridge LF, Nguyen AM, Heymsfield SB, Faith MS. Intentional weight loss and changes in symptoms of depression: a systematic review and meta-analysis. Int J Obes. 2011;35(11):1363-76. doi: 10.1038/ijo.2011.2
225. Warkentin LM, Das D, Majumdar SR, Johnson JA, Padwal RS. The effect of weight loss on health-related quality of life: systematic review and meta-analysis of randomized trials. Obes Rev. 2014;15(3):169-82. doi: 10.1111/obr.12113
226. Zhong P, Zeng H, Huang M, Fu W, Chen Z. Efficacy and safety of once-weekly semaglutide in adults with overweight or obesity: a meta-analysis. Endocrine. 2022;75(3):718-24. doi: 10.1007/s12020-021-02945-1
227. Hu Y, Zheng SL, Ye XL, Shi JN, Zheng XW, Pan HS, et al. Cost-effectiveness analysis of 4 GLP-1RAs in the treatment of obesity in a US setting. Ann Transl Med. 2022;10(3):152. doi: 10.21037/atm-22-200

Question: Pharmacological interventions compared to treated/untreated comparators for weight maintenance/loss in individuals with a mental health condition experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pharmacological interventions	treated/untreated comparators	Relative (95% CI)	Absolute (95% CI)		
Glucagon-like peptide-1 receptor agonists drug class (Liraglutide, 1.8mg per day) interventions vs any comparator (baseline to final end-point)												
1[a]	randomised trials	not serious	not serious	not serious	serious[b]	none	1/1 study found a positive effect of glucagon-like peptide-1 receptor agonists on weight maintenance/loss. Weight reduced by 2.4 kgs in the intervention group compared to a gain of 0.1 kgs in the comparator arm				⊕⊕⊕◯ Moderate	Glucagon-like peptide-1 receptor agonists drug class interventions likely reduce adiposity.

CI: confidence interval

Explanations

a. 1 study, with 1 intervention arm
b. -1 Imprecision due to small sample size (Total n<400)

People living with an eating disorder

QUESTION

Should interventions combining nutrition and physical activity vs. treated/untreated comparators be used for weight maintenance/loss in individuals with an eating disorder experiencing overweight or obesity?	
POPULATION:	People with an eating disorder living with overweight or obesity
INTERVENTION:	Combined nutrition and physical activity interventions (without sedentary behaviour interventions) vs untreated comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	There are significant bi-directional relationships between obesity and eating disorders, particularly bulimia nervosa and binge eating disorder (1). Obesity is associated with histories of eating disorders (1). Analysis of data from a nationally representative sample of US adults, for example, showed that people with overweight or obesity had greater odds of lifetime diagnoses of bulimia nervosa or binge-eating than those in other weight status groups (2). Eating disorders are also associated with histories of overweight and obesity (1). Among adolescents aged 9 to 22 years with eating disorder diagnoses characterized by dietary restriction and/or weight loss (e.g., anorexia nervosa), 36.7% had histories with BMIs above the 85th percentile (3). An analysis of data from Wave 6 of the Longitudinal Study of Australian Children showed that some self-reported symptoms of anorexia nervosa and bulimia nervosa were more prevalent among adolescents (14 to 15 years) with overweight and obesity than in other weight status groups (4). The estimated prevalences of one of two anorexia nervosa symptoms (fear of gaining weight or behaviours that interfere with weight gain) and all three bulimia nervosa symptoms (binge eating, overvaluation of weight, and engagement in compensatory behaviours) were higher among adolescents with overweight or obesity than those with normal weight or underweight (4). Analysis of data from statewide community samples of adults showed increases in the predicted prevalence of obesity and eating disorder behaviours in South Australia between 1995 to 2015 (5). Specifically, there were increases in the predicted prevalence of obesity (18.1% to 32.5%), binge eating (2.4% to 12.7%), very strict dieting/fasting (1.3% to 5.0%), obesity with comorbid binge eating (0.8% to 5.8%), and obesity with comorbid very strict dieting/fasting (0.2% to 2.3%) (5). Numerous factors may influence the association between obesity and eating disorders. Individual risk factors include genetics (e.g., the fat mass and obesity-associated gene), neuropsychological mechanisms,	In Australia, an estimated 5.1% of people aged 16 to 85 years experienced binge eating during their lifetimes (2020-21 figure) (216). Females were more likely to have experienced binge eating than males (7.4% versus 3.0%). The prevalence of lifetime binge eating among people aged 16 to 34 was higher than for people aged 65 to 85 (7.0% versus 2.1%). An experience of binge eating in the previous 12 months was more common among females aged 16 to 34 than all people aged 16 to 85 (5.6% versus 2.4%) (216).

	biochemical functions (e.g., the neuroendocrine system, serotonin), gut bacteria and immune system, psychological characteristics (e.g., low self-esteem, negative self-evaluation, emotional dysregulation, body satisfaction), and behaviour (e.g., dieting) (1). Environmental risk factors include family and peer teasing, perceived social pressure, bullying, frequent criticism, and images on social media or television that promote slimness and beauty ideals and contribute to body dissatisfaction (1). **Children and adolescents (2 to <18y)** <u>Blood pressure indicators</u> Prevalence of prehypertension (6), hypertension and elevated blood pressure (6-11) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (12). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (13, 14). <u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (6, 9-11). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (12). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (13, 15) and mortality (14, 15) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (14). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (6, 10, 11). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (10, 11). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (13-15). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (10) and risk of developing non-alcoholic fatty liver disease (6, 16-18) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural,	

	nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (19). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (20). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (21), and ovarian (21, 22) cancer during adulthood among women; and colorectal cancer (23) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (24). <u>Mental health</u> Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (10) and depression (10, 25) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (26). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (27). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (10). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (28). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (29). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (29). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (29). **Young and middle-aged adults (18 to <65y)** <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (30-41). Cardiovascular disease mortality increased with increasing weight (40, 42-44). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (45, 46), including ischemic stroke (45), and haemorrhagic stroke (45). Risk was also elevated for coronary artery disease (47, 48).	

Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (49). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (50).

Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (34, 51-53).

<u>Blood glucose level</u>
A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (54).

<u>Type 2 diabetes mellitus</u>
Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (38, 48, 55-70).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (34, 54, 71-74).

<u>Non-alcoholic fatty liver disease</u>
Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (75-80).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (81-83). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (81).

<u>Musculoskeletal conditions</u>
Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (84). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (85).

<u>Cancer</u>
When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (86, 87), thyroid (87-93), and blood cancers such as; lympho-haematopoietic (94) and diffuse large B-cell lymphoma (95, 96), multiple myeloma (87, 96-98), Hodgkin and non-Hodgkin lymphoma (87, 96), and leukemia (99, 100) (obesity only (101)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (70, 86, 87, 92, 98, 99, 102-107), gastroesophageal (108, 109), gastric (87, 92, 107, 110, 111), and stomach

	(70) cancers; and liver (70, 87, 92, 98, 109, 112-121), gallbladder (70, 87, 98, 99, 122-124), bile duct (125), pancreatic (70, 92, 98, 99, 109, 126-128), small intestinal (126), and colorectal (86, 87, 92, 98, 99, 109, 127, 129-146) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (70, 86, 87, 92, 98, 99, 109, 139, 147-151), and bladder (70, 87, 149, 150, 152-155)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (99) cancers, and total cancer risk was associated with increasing adiposity (156). Increased BMI in adulthood (≥18y) was protective against lung cancer (86, 157, 158), and pre-menopausal breast cancer (86, 159). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (160). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (161). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (87, 109, 162-165) (premenopausal (92, 166, 167) or postmenopausal (139) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (168). Risk of other gynaecological cancers also increased, including endometrial (86, 87, 98, 99, 136, 139, 169-172), uterine (70), and cervical cancers (87) (weak association with obesity (173)), as well as breast cancer (92, 99, 109, 136, 139, 156, 173-185). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (49). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (149, 186, 187), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (86, 188), while risk increased for development of advanced prostate cancer (109, 150, 188, 189) and prostate cancer mortality (190). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (191). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (192, 193), or depression (194, 195), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (191). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (196). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (197). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a	

	healthy body weight (198). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (199-203). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (204). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (205). **Older adults (≥65y)** Cardiovascular disease The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (206). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (207). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (208). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (208). Type 2 diabetes mellitus Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (209, 210). Musculoskeletal conditions Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (211, 212). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (213, 214). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (215). Cancer A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (159).	
Desirable Effects How substantial are the desirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	Evidence from narrative synthesis: 1 study (217) of participants living with a binge eating condition post-bariatric surgery unable to be included in a meta-analysis found in favour of combining nutrition and physical activity for weight maintenance/loss. Intervention arm gained 2.1% of total body weight versus 3.9% in the comparator arm. No studies in people with other eating disorders were identified. Additional desirable benefits: No evidence was identified in this population.	In people with binge eating disorders, decisions regarding weight management for individuals may change over time. Treatment of the eating disorder should be prioritised.

	The following evidence was taken from young and middle-aged adult population: Nutrition and physical activity interventions combined, showed favourable effects for cardiovascular events (218), type 2 diabetes risk (219), cancer risk (218), mental health (220), mortality (all cause, cardiovascular, and cancer mortality) (218), systolic (221, 222) and diastolic (222) blood pressure, fasting glucose (221), HbA1c levels (222, 223), and triglycerides (222). Women participating in combined nutrition and physical activity interventions had reduced incidence of type 2 diabetes and reduced systolic blood pressure (224). Additional desirable effects experienced by South Asians participating in combined nutrition and physical activity interventions included reduced diabetes incidence and reduced 2-hour glucose levels (225). Adults with prediabetes participating in combined nutrition and physical activity interventions had reduced incidence of diabetes and improved glycaemic control (226). The following evidence was taken from older adult population. Additional desirable effects experienced by older adults participating in nutrition and physical activity interventions included reduced total cholesterol (227). <u>Lived experience:</u> **Young and Middle-aged Adults (18-<65 years)** Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (228-231). Reduction in mental health symptoms including depression and anxiety (220, 232), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (233-237). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (238-242). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (242-245). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (246-249). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (246, 247). Increased physical activity was associated with psychological wellbeing, and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (196, 224, 250, 251). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (250, 251).	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (252), Healthy China Initiative (253), Finnish Diabetes Prevention Study (254)) overwhelmingly support positive health outcomes of physical activity and improved nutrition. The benefits of weight loss or maintenance on cardiometabolic outcomes were also considered when making judgement. In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (255). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (255).

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small	<u>Evidence from meta-analyses:</u> No evidence was identified in this population.	When people who are living with overweight or obesity

○ Moderate ○ Large ○ Varies ● Don't know	Additional undesirable benefits: No evidence was identified in this population. The following evidence was taken from young and middle-aged adult population: Decreased bone mineral density was reported as an adverse outcome experienced when undertaking a nutrition and physical activity intervention (221). Lived experience: **Young and Middle-aged Adults (18-<65 years)** Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (224, 240, 246). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (246, 247). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (251). Fears of embarrassment and failure during exercise activities were also reported (224, 244, 251, 256). Cultural and social expectations related to food and alcohol impacted adherence (240, 244) (257). Limited access to culturally appropriate and healthy foods (244), financial constraints (258), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (243, 250, 259-261).	and an eating disorder are participating in a behavioural weight loss intervention that incorporates diet change, clinical judgement and ongoing monitoring is essential to balance priorities for health care and to prevent worsening of eating disorder. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. The evidence is very uncertain about the effect of nutrition and physical activity interventions on adiposity in people with a binge eating disorder. No other information was identified for people with other eating disorders. No evidence available for the effect of sedentary behaviour interventions.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important	We have not sourced literature on the preferences and values of people living with an eating disorder and overweight or obesity in relation to receiving combined nutrition and physical activity treatment. However, the committee believes that since there are benefits, most people living	People experiencing binge eating disorder would likely value appropriate clinical treatment to assist weight

uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	with overweight or obesity and an eating disorder would opt for this treatment.	management. Treatment of the eating disorder should be prioritised. Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects is not known.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strengthening activities.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on resource requirements. Physical activity and nutrition interventions are widely available and often affordable for the wider population. However, interventions specific to people with eating disorders are not widely available and/or affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not sourced literature on required resources.	

Cost effectiveness Does the cost-effectiveness of the intervention favour the intervention or the comparison?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ● Varies ○ Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	The committee strongly believes that people living with disadvantage face lower health equity. Access to nutrition and physical activity interventions is typically unaffordable for disadvantaged populations, including people with binge eating disorders, as costs of nutritious foods, gym memberships, club fees, and equipment are borne by participants. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost programs, or when discussing the patient's care plan, practitioners should take into consideration whether the

		patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.
Acceptability Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know	We have not sourced literature on the acceptability of people living with an eating disorder receiving combined nutrition and physical activity treatments. However, the committee believes this intervention is likely to be acceptable to the majority of people living with overweight or obesity, and clinicians. Additional considerations for treatment for eating disorders are required.	There is a need for further research. Acceptability increases where interventions are individually tailored and culturally appropriate. Accessibility of nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ● Don't know	Literature on the feasibility of people living with an eating disorder receiving combined nutrition and physical activity interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Resourcing will be dependent on setting, intervention, location, and population.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**Don't know**
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	**Don't know**
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	**Don't know**

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Where clinically appropriate, combined nutrition and physical activity interventions, as part of a comprehensive approach to management of weight-related health and wellbeing, may be encouraged.

REFERENCES SUMMARY

1. Da Luz FQ, Hay P, Touyz S, Sainsbury A. Obesity with comorbid eating disorders: associated health risks and treatment approaches. Nutrients. 2018;10(7):829. doi: 10.3390/nu10070829
2. Udo T, Grilo CM. Prevalence and correlates of DSM-5–defined eating disorders in a nationally representative sample of U.S. adults. Biological Psychiatry. 2018;84(5):345-54. doi: 10.1016/j.biopsych.2018.03.014
3. Lebow J, Sim LA, Kransdorf LN. Prevalence of a history of overweight and obesity in sdolescents with restrictive eating disorders. J Adolesc Health. 2015;56(1):19-24. doi: 10.1016/j.jadohealth.2014.06.005
4. Hughes EK, Kerr JA, Patton GC, Sawyer SM, Wake M, Le Grange D, Azzopardi P. Eating disorder symptoms across the weight spectrum in Australian adolescents. Int J Eat Disord. 2019;52(8):885-94. doi: 10.1002/eat.23118
5. Da Luz FQ, Sainsbury A, Mannan H, Touyz S, Mitchison D, Hay P. Prevalence of obesity and comorbid eating disorder behaviors in South Australia from 1995 to 2015. Int J Obes. 2017;41(7):1148-53. doi: 10.1038/ijo.2017.79
6. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
7. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
8. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
9. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
10. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
11. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
12. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
13. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
14. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
15. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
16. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
17. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
18. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
19. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
20. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067

21. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
22. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
23. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
24. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
25. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
26. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
27. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
28. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
29. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
30. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
31. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
32. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
33. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
34. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
35. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
36. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
37. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
38. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
39. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
40. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
41. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
42. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
43. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247

44. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
45. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
46. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
47. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
48. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
49. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
50. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
51. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
52. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
53. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
54. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
55. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
56. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
57. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
58. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
59. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
60. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
61. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
62. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
63. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
64. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
65. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218

66. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
67. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
68. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
69. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
70. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
71. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
72. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
73. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
74. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
75. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
76. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
77. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
78. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
79. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
80. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
81. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
82. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
83. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
84. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
85. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
86. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
87. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
88. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
89. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
90. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
91. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321

92. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
93. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
94. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
95. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
96. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
97. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
98. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
99. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
100. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
101. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
102. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
103. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
104. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
105. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
106. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
107. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
108. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
109. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
110. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
111. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
112. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
113. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
114. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
115. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176

116. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
117. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
118. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
119. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
120. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
121. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
122. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
123. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
124. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
125. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
126. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
127. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
128. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
129. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
130. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
131. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
132. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
133. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
134. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
135. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
136. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
137. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
138. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
139. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
140. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706

141. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
142. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
143. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
144. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
145. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
146. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
147. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
148. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
149. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
150. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
151. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
152. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
153. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
154. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
155. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
156. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
157. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
158. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
159. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
160. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
161. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
162. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
163. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8

164. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
165. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
166. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
167. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
168. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
169. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
170. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
171. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
172. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
173. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
174. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
175. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
176. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
177. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
178. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
179. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
180. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
181. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
182. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
183. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
184. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
185. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
186. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
187. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
188. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
189. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64

190. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
191. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
192. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
193. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
194. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
195. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
196. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
197. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
198. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
199. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
200. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
201. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
202. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
203. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
204. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
205. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
206. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
207. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
208. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
209. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
210. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
211. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
212. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013

213. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
214. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
215. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
216. Australian Bureau of Statistics. National study of mental health and wellbeing 2020-21 [Internet] Canberra: ABS; 2022 [cited 2024 August 14]. Available from: https://www.abs.gov.au/statistics/health/mental-health/national-study-mental-health-and-wellbeing/2020-21.
217. Grilo CM, Ivezaj V, Duffy AJ, Gueorguieva R. 24-month follow-up of randomized controlled trial of guided-self-help for loss-of-control eating after bariatric surgery. Int J Eat Disord. 2022;55(11):1521-31. doi: 10.1002/eat.23804
218. Ma C, Avenell A, Bolland M, Hudson J, Stewart F, Robertson C, et al. Effects of weight loss interventions for adults who are obese on mortality, cardiovascular disease, and cancer: systematic review and meta-analysis. BMJ. 2017;359:j4849. doi: 10.1136/bmj.j4849
219. LeBlanc ES, Patnode CD, Webber EM, Redmond N, Rushkin M, O'Connor EA. Behavioral and pharmacotherapy weight loss interventions to prevent obesity-related morbidity and mortality in adults: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2018;320(11):1172-91. doi: 10.1001/jama.2018.7777
220. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
221. Leblanc ES, O'Connor E, Whitlock EP, Patnode CD, Kapka T. Effectiveness of primary care-relevant treatments for obesity in adults: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med. 2011;155(7):434-47. doi: 10.7326/0003-4819-155-7-201110040-00006
222. Dombrowski SU, Avenell A, Sniehott FF. Behavioural interventions for obese adults with additional risk factors for morbidity: systematic review of effects on behaviour, weight and disease risk factors. Obes Facts. 2010;3(6):377-96. doi: 10.1159/000323076
223. Johnson M, Jones R, Freeman C, Woods HB, Gillett M, Goyder E, Payne N. Can diabetes prevention programmes be translated effectively into real-world settings and still deliver improved outcomes? A synthesis of evidence. Diabet Med. 2013;30(1):3-15. doi: 10.1111/dme.12018
224. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
225. Jenum AK, Brekke I, Mdala I, Muilwijk M, Ramachandran A, Kjøllesdal M, et al. Effects of dietary and physical activity interventions on the risk of type 2 diabetes in South Asians: meta-analysis of individual participant data from randomised controlled trials. Diabetologia. 2019;62(8):1337-48. doi: 10.1007/s00125-019-4905-2
226. Kerrison G, Gillis RB, Jiwani SI, Alzahrani Q, Kok S, Harding SE, et al. The effectiveness of lifestyle adaptation for the prevention of prediabetes in adults: a systematic review. J Diabetes Res. 2017;2017:8493145. doi: 10.1155/2017/8493145
227. Witham MD, Avenell A. Interventions to achieve long-term weight loss in obese older people: a systematic review and meta-analysis. Age Ageing. 2010;39(2):176-84. doi: 10.1093/ageing/afp251
228. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
229. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
230. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
231. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
232. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
233. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6

234. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
235. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
236. Palavras MA, Hay P, Filho CADS, Claudino A. The fffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
237. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
238. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
239. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
240. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
241. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657
242. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
243. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
244. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
245. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
246. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
247. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
248. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
249. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
250. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
251. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
252. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
253. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
254. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
255. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
256. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114

257. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
258. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
259. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
260. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
261. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition and physical activity compared to treated/untreated comparators for weight maintenance/loss in individuals with an eating disorder experiencing overweight or obesity

Certainty assessment							Impact	Certainty	Evidence statement
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Nutrition and physical activity interventions vs **untreated comparator (baseline to 12 months)** – Narrative synthesis									
1[a]	randomised trials	very serious[b]	not serious	not serious	serious[c]	none	1/1 study found in favour of combining nutrition and physical activity for weight maintenance/loss. Intervention arm gained 2.1% of total body weight versus 3.9% in the comparator arm	⨁◯◯◯ Very low	The evidence is very uncertain about the effect of this intervention on adiposity.

CI: confidence interval

Explanations

a. 1 study, with 1 intervention arm
b. -2 using RoB-2 risk of bias rated High for all outcomes
c. -1 Imprecision due to small sample size (Total n<400)

QUESTION

Should interventions combining nutrition, physical activity and psychological intervention vs. treated/untreated comparators be used for weight maintenance/loss in individuals with an eating disorder experiencing overweight or obesity?	
POPULATION:	People with an eating disorder living with overweight or obesity
INTERVENTION:	Combined nutrition, physical activity, and psychological interventions vs any comparator (baseline to 12 months)
COMPARISON:	Treated/untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	There are significant bi-directional relationships between obesity and eating disorders, particularly bulimia nervosa and binge eating disorder (1). Obesity is associated with histories of eating disorders (1). Analysis of data from a nationally representative sample of US adults, for example, showed that people with overweight or obesity had greater odds of lifetime diagnoses of bulimia nervosa or binge-eating than those in other weight status groups (2). Eating disorders are also associated with histories of overweight and obesity (1). Among adolescents aged 9 to 22 years with eating disorder diagnoses characterized by dietary restriction and/or weight loss (e.g., anorexia nervosa), 36.7% had histories with BMIs above the 85th percentile (3). An analysis of data from Wave 6 of the Longitudinal Study of Australian Children showed that some self-reported symptoms of anorexia nervosa and bulimia nervosa were more prevalent among adolescents (14 to 15 years) with overweight and obesity than in other weight status groups (4). The estimated prevalences of one of two anorexia nervosa symptoms (fear of gaining weight or behaviours that interfere with weight gain) and all three bulimia nervosa symptoms (binge eating, overvaluation of weight, and engagement in compensatory behaviours) were higher among adolescents with overweight or obesity than those with normal weight or underweight (4). Analysis of data from statewide community samples of adults showed increases in the predicted prevalence of obesity and eating disorder behaviours in South Australia between 1995 to 2015 (5). Specifically, there were increases in the predicted prevalence of obesity (18.1% to 32.5%), binge eating (2.4% to 12.7%), very strict dieting/fasting (1.3% to 5.0%), obesity with comorbid binge eating (0.8% to 5.8%), and obesity with comorbid very strict dieting/fasting (0.2% to 2.3%) (5). Numerous factors may influence the association between obesity and eating disorders. Individual risk factors include genetics (e.g., the fat mass and obesity-associated gene), neuropsychological mechanisms, biochemical functions (e.g., the neuroendocrine system, serotonin), gut bacteria and immune system, psychological characteristics (e.g., low self-	In Australia, an estimated 5.1% of people aged 16 to 85 years experienced binge eating during their lifetimes (2020-21 figure) (216). Females were more likely to have experienced binge eating than males (7.4% versus 3.0%). The prevalence of lifetime binge eating among people aged 16 to 34 was higher than for people aged 65 to 85 (7.0% versus 2.1%). An experience of binge eating in the previous 12 months was more common among females aged 16 to 34 than all people aged 16 to 85 (5.6% versus 2.4%).

	esteem, negative self-evaluation, emotional dysregulation, body satisfaction), and behaviour (e.g., dieting) (1). Environmental risk factors include family and peer teasing, perceived social pressure, bullying, frequent criticism, and images on social media or television that promote slimness and beauty ideals and contribute to body dissatisfaction (1). **Children and adolescents (2 to <18y)** Blood pressure indicators Prevalence of prehypertension (6), hypertension and elevated blood pressure (6-11) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (12). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (13, 14). Blood lipid profile Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (6, 9-11). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (12). Cardiovascular disease Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (13, 15) and mortality (14, 15) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (14). Blood glucose level Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (6, 10, 11). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (10, 11). Type 2 diabetes mellitus Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (13-15). Non-alcoholic fatty liver disease Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (10) and risk of developing non-alcoholic fatty liver disease (6, 16-18) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children	

and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (19).

Musculoskeletal conditions

Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (20).

Cancer

Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (21), and ovarian (21, 22) cancer during adulthood among women; and colorectal cancer (23) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (24).

Mental health

Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (10) and depression (10, 25) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (26). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (27).

Health-related quality of life ratings

Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (10). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (28).

Reproductive health

Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (29). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (29). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (29).

Young and middle-aged adults (18 to <65y)

Cardiovascular disease

Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (30-41). Cardiovascular disease mortality increased with increasing weight (40, 42-44). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (45, 46), including ischemic stroke (45), and haemorrhagic stroke (45). Risk was also elevated for coronary artery disease (47, 48).

Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or ‘other’ causes, compared to healthy weight survivors (49). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (50).

Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants’ risk of mortality from cardiovascular disease decreased (34, 51-53).

Blood glucose level

A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (54).

Type 2 diabetes mellitus

Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (38, 48, 55-70).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (34, 54, 71-74).

Non-alcoholic fatty liver disease

Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (75-80).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (81-83). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (81).

Musculoskeletal conditions

Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (84). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (85).

Cancer

When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (86, 87), thyroid (87-93), and blood cancers such as; lympho-haematopoietic (94) and diffuse large B-cell lymphoma (95, 96), multiple myeloma (87, 96-98), Hodgkin and non-Hodgkin lymphoma (87, 96), and leukemia (99, 100) (obesity only (101)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (70, 86, 87, 92, 98, 99, 102-107), gastroesophageal (108, 109), gastric (87, 92, 107, 110, 111), and stomach

	(70) cancers; and liver (70, 87, 92, 98, 109, 112-121), gallbladder (70, 87, 98, 99, 122-124), bile duct (125), pancreatic (70, 92, 98, 99, 109, 126-128), small intestinal (126), and colorectal (86, 87, 92, 98, 99, 109, 127, 129-146) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (70, 86, 87, 92, 98, 99, 109, 139, 147-151), and bladder (70, 87, 149, 150, 152-155)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (99) cancers, and total cancer risk was associated with increasing adiposity (156). Increased BMI in adulthood (≥18y) was protective against lung cancer (86, 157, 158), and pre-menopausal breast cancer (86, 159). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (160). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (161). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (87, 109, 162-165) (premenopausal (92, 166, 167) or postmenopausal (139) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (168). Risk of other gynaecological cancers also increased, including endometrial (86, 87, 98, 99, 136, 139, 169-172), uterine (70), and cervical cancers (87) (weak association with obesity (173)), as well as breast cancer (92, 99, 109, 136, 139, 156, 173-185). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (49). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (149, 186, 187), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (86, 188), while risk increased for development of advanced prostate cancer (109, 150, 188, 189) and prostate cancer mortality (190). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (191). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (192, 193), or depression (194, 195), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (191). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (196). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (197). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a	

	healthy body weight (198). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (199-203). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (204). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (205). **Older adults (≥65y)** <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (206). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (207). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (208). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (208). <u>Type 2 diabetes mellitus</u> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (209, 210). <u>Musculoskeletal conditions</u> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (211, 212). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (213, 214). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (215). <u>Cancer</u> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (159).	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	<u>Evidence from narrative synthesis:</u> From 1 study (217) with 47 intervention participants and 49 comparator participants, evidence demonstrated a small important effect size of Hedges' g 0.25 lower (0.74 lower to 0.23 higher) in nutrition, physical activity, and psychological interventions versus any comparator. <u>Additional desirable effects:</u> No evidence was identified in this population	In people with binge eating disorders, decisions regarding weight management for individuals may change over time. Treatment of the binge eating disorder should take priority.

	The following evidence was taken from the young and middle-aged adult population: In men only, nutrition, physical activity, and behaviour therapy (e.g., initiatives based on social cognitive theory) interventions, showed favourable outcomes for systolic and diastolic blood pressure, plasma glucose, and blood lipids (HDL-C, LDL-C, triglycerides, and total cholesterol) (218). Lived experience: **Children and Adolescents:** Two reviews (219, 220) reported change in eating disorder behaviours in children and adolescents (7-18 years) following interventions that combined nutrition, physical activity and psychological treatments. Eating disorder risk, bulimic symptoms, emotional eating, and binge eating were reduced post-intervention in one review (220). A second review (219) reported mixed results. Disordered eating behaviour (including dietary restraint, binge eating) decreased or were unchanged, while dietary restraint was increased or unchanged. One additional review found binge eating and loss of control (BE/LOC) behaviours significantly decreased following weight-loss interventions (all types of interventions), and a greater decrease in BE/LOC was associated with improved weight loss (221). **Young and middle-aged adults (18-<65 years)** Two reviews (222, 223) reported change in eating disorder symptoms in young and middle-aged adults following psychological interventions. Cognitive behavioural therapy (CBT) was found to reduce short-term binge eating compared to behavioural weight loss therapy (BWLT) (223). Non-significant changes were found for binge eating, emotional eating, external eating and restraint eating following Acceptance based therapy (ACT) (222). One additional study (224) found weight-neutral approaches resulted in greater improvement in bulimia (P=0.02) compared to weight loss interventions, with no significant differences observed for any other outcome. The following evidence was taken from the young and middle-aged adult population: Studies of behavioural interventions for adults have shown improvements in health-related quality of life, including vitality, mental health, physical function, and reduced body pain (225-228). Reduction in mental health symptoms including depression and anxiety (229, 230), and eating disorder problems including bulimia, binge eating, and emotional eating have been reported (222-224, 231, 232). Social support and positive engagement from programme facilitators were shown to influence successful behaviour change (233-237). Participants were motivated by a desire for improved health, self-image, and health-related quality of life, and when weight loss was achieved experienced a greater sense of perceived control, self-efficacy, and improved social functioning (237-240). Strategies such as group interventions, goal setting, food/activity logs, and daily self-weighing were important for supporting behaviour change and maintaining motivation for adhering to interventions (241-244). Developing strategies to overcome emotional eating and managing social events centred on food were helpful in sustaining weight loss (241, 242). Increased physical activity was associated with psychological wellbeing,	Research findings from multiple, large community-based longitudinal studies (e.g., the Diabetes Prevention Program (USA) (247), Healthy China Initiative (248), Finnish Diabetes Prevention Study (249)) overwhelmingly support positive health outcomes of physical activity and improved nutrition. In young and middle-aged adults taking part in weight loss nutrition interventions, lean mass loss was small (i.e. fat free mass losses ranged between 1.0 and 1.5 kg, and skeletal muscle mass losses ranged between 0.9 kg–1.7 kg) (250). Similarly, in adults taking part in weight loss physical activity interventions, loss of skeletal muscle mass was likely to contribute to the preservation of lean mass, particularly skeletal muscle mass (250).

	and enjoyment, and improvements in motivation, body image, self-confidence, and self-worth (196, 218, 245, 246). Support for forming exercise habits, accountability, and maintaining motivation facilitated adherence. Friends, family, and supportive workplaces were important enablers for adhering to behavioural interventions (245, 246).	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	<u>Evidence from meta-analyses:</u> No evidence was identified in this population. <u>Additional undesirable effects:</u> No evidence was identified in this population. <u>Lived experience:</u> **Young and middle-aged adults (18-<65 years)** Adults engaged in behavioural interventions who experienced unsuccessful attempts at weight loss reported negative impacts on health-related quality of life and behaviours. Barriers to adherence included unsupportive social environments, such as negative perceptions and comments from others around them, availability of unhealthy food at work, and sedentary job roles (218, 235, 241). Participants described challenges in prioritising and maintaining healthy behaviours, which could result in feelings of resentment, emotional distress, and deprivation from dieting and food restrictions (241, 242). Engaging in physical activity components was difficult due to physical limitations, pain, poor body image, low self-esteem, and fears of using equipment that was not suitable for their body size (246). Fears of embarrassment and failure during exercise activities were also reported (218, 239, 246, 251). Cultural and social expectations related to food and alcohol impacted adherence (235, 239) (252). Limited access to culturally appropriate and healthy foods (239), financial constraints (253), and reluctance to share information with healthcare providers due to weight bias and stigma also contributed to the challenges in engaging with interventions (238, 245, 254-256).	When people who are living with overweight or obesity and an eating disorder are participating in a behavioural weight loss intervention that incorporates diet change, clinical judgement and ongoing monitoring is essential to balance priorities for health care and to prevent worsening of eating disorder. A low but real risk of incidental musculoskeletal injury exists for people with overweight or obesity during physical activity. Appropriate individually tailored and monitored exercise programs, that include realistic goal setting, should be developed for people living with overweight or obesity with a goal to minimise risk of injury and stigma, while protecting mental health and engagement. Internalised and external stigma often reduces engagement with physical activity programs and needs to be considered during program development.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Refer to end of Evidence-to-Decision framework for GRADE Summary of Findings (SoF) table. Nutrition, physical activity, and psychological interventions may reduce adiposity slightly in people with eating disorders.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on patients' preferences and values in relation to receiving combined nutrition, physical activity, and psychological treatment. However, the committee believes that since there are benefits, many people living with overweight or obesity and an eating disorder would opt for this treatment.	People experiencing binge eating disorder would likely value appropriate clinical treatment to assist weight management. However, treatment of the eating disorder should be prioritised. Some people living with overweight or obesity (possibly including those guided by a weight neutral approach philosophy) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects probably favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. Lean mass loss may be ameliorated with exercise, particularly strength training.

Resources required

How large are the resource requirements (costs)?"

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on resource requirements. Combined nutrition, physical activity and psychological interventions are widely available and affordable. However, interventions specific to people with eating disorders are not widely available and/or affordable.	Dietitians are expensive for patients via the private system, and there is a lack of availability through public health system. Participants reported financial barriers to structured physical activity, including expensive gym memberships, equipment, and clothing. Long-term psychological care is often needed, and

		treatment is unlikely to be one-off. This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Very low o Low o Moderate o High ● No included studies	We have not sourced literature on required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Favours the comparison o Probably favours the comparison o Does not favour either the intervention or the comparison o Probably favours the intervention o Favours the intervention o Varies ● No included studies	No evidence on the cost effectiveness of this intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
o Reduced o Probably reduced o Probably no impact o Probably increased o Increased o Varies ● Don't know	We have not sourced literature about how health equity would be impacted through delivery of this intervention.	The committee strongly believes that people living with disadvantage face lower health equity. Access to nutrition and physical activity interventions is typically unaffordable for disadvantaged populations, including people with binge eating disorders, as costs of nutritious foods, gym

		memberships, club fees and equipment are often borne by participants. High cost of psychological care and long wait times may make treatment prohibitive for some people, decreasing health equity. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available, low-cost programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment. Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of people living with an eating disorder receiving combined nutrition, physical activity, and psychological treatments. However, the committee believes this intervention is likely to be acceptable to many people with overweight or obesity and an eating disorder, and clinicians.	Need for further research Acceptability increases where interventions are individually tailored and culturally appropriate. Accessibility of

		nutritious, affordable food increases acceptability. Mental health of the participant should be considered and monitored.
Feasibility Is the intervention feasible to implement?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of people living with an eating disorder receiving nutrition, physical activity and psychological interventions was not sourced. This treatment type is likely to be practicable, however. Inconsistency in accessing the range of resources required to implement this treatment may vary across Australia, resulting in reduced feasibility.	Once research evidence is available for people with a binge eating disorder, feasibility could be more accurately assessed.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	**Don't know**
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation
<u>Consensus statement due to limited evidence:</u> Where clinically appropriate, combined nutrition, physical activity, and psychological interventions (to support weight management), as part of a comprehensive approach to management of weight-related health and wellbeing, are encouraged.

REFERENCES SUMMARY

1. Da Luz FQ, Hay P, Touyz S, Sainsbury A. Obesity with comorbid eating disorders: associated health risks and treatment approaches. Nutrients. 2018;10(7):829. doi: 10.3390/nu10070829
2. Udo T, Grilo CM. Prevalence and correlates of DSM-5–defined eating disorders in a nationally representative sample of U.S. adults. Biological Psychiatry. 2018;84(5):345-54. doi: 10.1016/j.biopsych.2018.03.014
3. Lebow J, Sim LA, Kransdorf LN. Prevalence of a history of overweight and obesity in sdolescents with restrictive eating disorders. J Adolesc Health. 2015;56(1):19-24. doi: 10.1016/j.jadohealth.2014.06.005
4. Hughes EK, Kerr JA, Patton GC, Sawyer SM, Wake M, Le Grange D, Azzopardi P. Eating disorder symptoms across the weight spectrum in Australian adolescents. Int J Eat Disord. 2019;52(8):885-94. doi: 10.1002/eat.23118
5. Da Luz FQ, Sainsbury A, Mannan H, Touyz S, Mitchison D, Hay P. Prevalence of obesity and comorbid eating disorder behaviors in South Australia from 1995 to 2015. Int J Obes. 2017;41(7):1148-53. doi: 10.1038/ijo.2017.79
6. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
7. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
8. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
9. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
10. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
11. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
12. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
13. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
14. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
15. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
16. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
17. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
18. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
19. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
20. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067

21. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
22. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
23. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
24. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
25. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
26. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
27. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
28. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
29. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
30. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
31. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
32. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
33. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
34. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
35. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
36. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
37. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
38. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
39. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
40. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
41. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
42. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
43. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247

44. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
45. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
46. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
47. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
48. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
49. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
50. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
51. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
52. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
53. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
54. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
55. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
56. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
57. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
58. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
59. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
60. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
61. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
62. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
63. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
64. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
65. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218

66. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
67. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
68. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
69. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
70. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
71. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
72. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
73. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
74. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
75. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
76. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
77. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
78. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
79. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
80. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
81. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
82. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
83. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
84. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
85. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
86. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
87. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
88. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
89. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
90. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
91. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321

92. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
93. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
94. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
95. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
96. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
97. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
98. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
99. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
100. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
101. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
102. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
103. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
104. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
105. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
106. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
107. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
108. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
109. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
110. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
111. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
112. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
113. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
114. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
115. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176

116. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
117. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
118. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
119. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
120. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
121. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
122. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
123. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
124. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
125. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
126. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
127. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
128. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
129. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
130. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
131. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
132. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
133. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
134. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
135. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
136. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1
137. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
138. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
139. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
140. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706

141. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
142. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
143. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
144. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
145. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
146. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
147. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
148. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
149. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
150. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
151. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
152. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
153. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
154. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
155. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
156. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
157. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
158. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
159. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
160. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037
161. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
162. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
163. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
164. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207

165. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
166. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
167. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
168. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
169. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
170. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
171. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
172. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
173. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
174. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
175. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
176. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
177. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
178. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
179. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
180. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
181. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
182. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
183. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
184. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987
185. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
186. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
187. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
188. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
189. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
190. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325

191. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
192. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
193. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
194. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
195. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
196. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
197. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
198. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
199. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
200. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
201. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
202. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
203. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
204. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
205. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
206. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
207. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
208. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
209. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
210. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
211. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
212. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
213. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
214. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1

215. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
216. Australian Bureau of Statistics. National study of mental health and wellbeing 2020-21 [Internet] Canberra: ABS; 2022 [cited 2024 August 14]. Available from: https://www.abs.gov.au/statistics/health/mental-health/national-study-mental-health-and-wellbeing/2020-21.
217. Cesa GL, Manzoni GM, Bacchetta M, Castelnuovo G, Conti S, Gaggioli A, et al. Virtual reality for enhancing the cognitive behavioral treatment of obesity with binge eating disorder: randomized controlled study with one-year follow-up. J Med Internet Res. 2013;15(6):e113. doi: 10.2196/jmir.2441
218. Robertson C, Archibald D, Avenell A, Douglas F, Hoddinott P, van Teijlingen E, et al. Systematic reviews of and integrated report on the quantitative, qualitative and economic evidence base for the management of obesity in men. Health Technol Assess. 2014;18(35). doi: 10.3310/hta18350
219. House ET, Gow ML, Lister NB, Baur LA, Garnett SP, Paxton SJ, Jebeile H. Pediatric weight management, dietary restraint, dieting, and eating disorder risk: a systematic review. Nutr Rev. 2021;79(10):1114-33. doi: 10.1093/nutrit/nuaa127
220. Jebeile H, Gow ML, Baur LA, Garnett SP, Paxton SJ, Lister NB. Treatment of obesity, with a dietary component, and eating disorder risk in children and adolescents: a systematic review with meta-analysis. Obes Rev. 2019;20(9):1287-98. doi: 10.1111/obr.12866
221. Moustafa AF, Quigley KM, Wadden TA, Berkowitz RI, Chao AM. A systematic review of binge eating, loss of control eating, and weight loss in children and adolescents. Obesity. 2021;29(8):1259-71. doi: 10.1002/oby.23185
222. Chew HSJ, Chng S, Rajasegaran NN, Choy KH, Chong YY. Effectiveness of acceptance and commitment therapy on weight, eating behaviours and psychological outcomes: a systematic review and meta-analysis. Eat Weight Disord. 2023;28(1):6. doi: 10.1007/s40519-023-01535-6
223. Palavras MA, Hay P, Filho CADS, Claudino A. The ffficacy of psychological therapies in reducing weight and binge eating in people with bulimia nervosa and binge eating disorder who are overweight or obese-a critical synthesis and meta-analyses. Nutrients. 2017;9(3). doi: 10.3390/nu9030299
224. Dugmore JA, Winten CG, Niven HE, Bauer J. Effects of weight-neutral approaches compared with traditional weight-loss approaches on behavioral, physical, and psychological health outcomes: a systematic review and meta-analysis. Nutr Rev. 2020;78(1):39-55. doi: 10.1093/nutrit/nuz020
225. Baillot A, Romain AJ, Boisvert-Vigneault K, Audet M, Baillargeon JP, Dionne IJ, et al. Effects of lifestyle interventions that include a physical activity component in class II and III obese individuals: a systematic review and meta-analysis. PLoS ONE. 2015;10(4):e0119017. doi: 10.1371/journal.pone.0119017
226. Buckell J, Mei XW, Clarke P, Aveyard P, Jebb SA. Weight loss interventions on health-related quality of life in those with moderate to severe obesity: findings from an individual patient data meta-analysis of randomized trials. Obes Rev. 2021;22(11):e13317. doi: 10.1111/obr.13317
227. Carraça EV, Encantado J, Battista F, Beaulieu K, Blundell JE, Busetto L, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: a systematic review and meta-analysis. Obes Rev. 2021;22 Suppl 4:e13261. doi: 10.1111/obr.13261
228. Dehghan Ghahfarokhi A, Vosadi E, Barzegar H, Saatchian V. The effect of wearable and smartphone applications on physical activity, quality of life, and cardiovascular health outcomes in overweight/obese adults: a systematic review and meta-analysis of randomized controlled trials. Biol Res Nurs. 2022;24(4):503-18. doi: 10.1177/10998004221099556
229. Jones RA, Lawlor ER, Birch JM, Patel MI, Werneck AO, Hoare E, et al. The impact of adult behavioural weight management interventions on mental health: a systematic review and meta-analysis. Obes Rev. 2021;22(4):e13150. doi: 10.1111/obr.13150
230. van Dammen L, Wekker V, de Rooij SR, Groen H, Hoek A, Roseboom TJ. A systematic review and meta-analysis of lifestyle interventions in women of reproductive age with overweight or obesity: the effects on symptoms of depression and anxiety. Obes Rev. 2018;19(12):1679-87. doi: 10.1111/obr.12752
231. Jiang Z, Zhang G, Huang J, Shen C, Cai Z, Yin X, et al. A systematic review of body contouring surgery in post-bariatric patients to determine its prevalence, effects on quality of life, desire, and barriers. Obes Rev. 2021;22(5):e13201. doi: 10.1111/obr.13201
232. Taghavi SA, van Wely M, Jahanfar S, Bazarganipour F. Pharmacological and non-pharmacological strategies for obese women with subfertility. Cochrane Database Syst Rev. 2021;3:CD012650. doi: 10.1002/14651858.CD012650.pub2
233. Anand VV, Zhe ELC, Chin YH, Lim WH, Goh RSJ, Lin C, et al. Barriers and facilitators to engagement with a weight management intervention in Asian patients with overweight or obesity: a systematic review. Endocr Pract. 2023;29(5):398-407. doi: 10.1016/j.eprac.2022.10.006
234. Melendez-Torres GJ, Sutcliffe K, Burchett HED, Rees R, Richardson M, Thomas J. Weight management programmes: re-analysis of a systematic review to identify pathways to effectiveness. Health Expect. 2018;21(3):574-84. doi: 10.1111/hex.12667
235. Neve KL, Isaacs A. How does the food environment influence people engaged in weight management? A systematic review and thematic synthesis of the qualitative literature. Obes Rev. 2022;23(3):e13398. doi: 10.1111/obr.13398
236. Sutcliffe K, Melendez-Torres GJ, Burchett HED, Richardson M, Rees R, Thomas J. The importance of service-users' perspectives: a systematic review of qualitative evidence reveals overlooked critical features of weight management programmes. Health Expect. 2018;21(3):563-73. doi: 10.1111/hex.12657

237. Tay A, Hoeksema H, Murphy R. Uncovering barriers and facilitators of weight loss and weight loss maintenance: insights from qualitative research. Nutrients. 2023;15(5):1297. doi: 10.3390/nu15051297
238. Avenell A, Robertson C, Skea Z, Jacobsen E, Boyers D, Cooper D, et al. Bariatric surgery, lifestyle interventions and orlistat for severe obesity: the REBALANCE mixed-methods systematic review and economic evaluation. Health Technol Assess. 2018;22(68). doi: 10.3310/hta22680
239. Farrell E, Hollmann E, le Roux CW, Bustillo M, Nadglowski J, McGillicuddy D. The lived experience of patients with obesity: a systematic review and qualitative synthesis. Obes Rev. 2021;22(12):e13334. doi: 10.1111/obr.13334
240. Spreckley M, Seidell J, Halberstadt J. Perspectives into the experience of successful, substantial long-term weight-loss maintenance: a systematic review. Int J Qual Stud Health Well-being. 2021;16(1):1862481. doi: 10.1080/17482631.2020.1862481
241. Greaves C, Poltawski L, Garside R, Briscoe S. Understanding the challenge of weight loss maintenance: a systematic review and synthesis of qualitative research on weight loss maintenance. Health Psychol Rev. 2017;11(2):145-63. doi: 10.1080/17437199.2017.1299583
242. Hartmann-Boyce J, Boylan AM, Jebb SA, Fletcher B, Aveyard P. Cognitive and behavioural strategies for self-directed weight loss: systematic review of qualitative studies. Obes Rev. 2017;18(3):335-49. doi: 10.1111/obr.12500
243. Hartmann-Boyce J, Nourse R, Boylan A-M, Jebb SA, Aveyard P. Experiences of reframing during self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Appl Psychol Health Well-Being. 2018;10(2):309-29. doi: 10.1111/aphw.12132
244. Hartmann-Boyce J, Boylan A-M, Jebb SA, Aveyard P. Experiences of self-monitoring in self-directed weight loss and weight loss maintenance: systematic review of qualitative studies. Qual Health Res. 2019;29(1):124-34. doi: 10.1177/1049732318784815
245. Skea ZC, Aceves-Martins M, Robertson C, De Bruin M, Avenell A, on behalf of the REBALANCE team. Acceptability and feasibility of weight management programmes for adults with severe obesity: a qualitative systematic review. BMJ Open. 2019;9(9):e029473. doi: 10.1136/bmjopen-2019-029473
246. Toft BS, Uhrenfeldt L. The lived experiences of being physically active when morbidly obese: a qualitative systematic review. Int J Qual Stud Health Well-being. 2015;10(1):28577. doi: 10.3402/qhw.v10.28577
247. Diabetes Prevention Program Research Group. Long-term effects of lifestyle intervention or metformin on diabetes development and microvascular complications over 15-year follow-up: the Diabetes Prevention Program Outcomes Study. Lancet Diabetes Endocrinol. 2015;3(11):866-75. doi: 10.1016/s2213-8587(15)00291-0
248. Wang L, Wang H, Wang Z, Jiang H, Li W, Wang S, et al. Interpretation of Healthy Diet Campaign in Healthy China Initiative 2019-2030. China CDC Wkly. 2021;3(16):346-9. doi: 10.46234/ccdcw2021.092
249. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, et al. The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care. 2003;26(12):3230-6. doi: 10.2337/diacare.26.12.3230
250. McCarthy D, Berg A. Weight Loss Strategies and the Risk of Skeletal Muscle Mass Loss. Nutrients. 2021;13(7). doi: 10.3390/nu13072473
251. Baillot A, Chenail S, Barros Polita N, Simoneau M, Libourel M, Nazon E, et al. Physical activity motives, barriers, and preferences in people with obesity: a systematic review. PLoS ONE. 2021;16(6):e0253114. doi: 10.1371/journal.pone.0253114
252. Termannsen A-D, Varming A, van Elst C, Bjerre N, Nørgaard O, Hempler NF, et al. Feasibility of time-restricted eating in individuals with overweight, obesity, prediabetes, or type 2 diabetes: a systematic scoping review. Obesity. 2023;31(6):1463-85. doi: 10.1002/oby.23743
253. Lee C, Piernas C, Stewart C, Michalopoulou M, Hajzadeh A, Edwards R, et al. Identifying effective characteristics of behavioral weight management interventions for people with serious mental illness: a systematic review with a qualitative comparative analysis. Obes Rev. 2022;23(1):e13355. doi: 10.1111/obr.13355
254. Ananthakumar T, Jones NR, Hinton L, Aveyard P. Clinical encounters about obesity: systematic review of patients' perspectives. Clin Obes. 2020;10(1):e12347. doi: 10.1111/cob.12347
255. Mold F, Forbes A. Patients' and professionals' experiences and perspectives of obesity in health-care settings: a synthesis of current research. Health Expect. 2013;16(2):119-42. doi: 10.1111/j.1369-7625.2011.00699.x
256. Alberga AS, Edache IY, Forhan M, Russell-Mayhew S. Weight bias and health care utilization: a scoping review. Prim Health Care Res Dev. 2019;20:e116. doi: 10.1017/S1463423619000227

Question: Interventions combining nutrition, physical activity and psychological intervention compared to treated/untreated comparators for weight maintenance/loss in individuals with an eating disorder experiencing overweight or obesity

Certainty assessment							№ of patients		Effect		Certainty	Evidence statement
№ of studies	Study design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	Other **considerations**	interventions **combining nutrition, physical activity, and psychological** intervention	treated/untreated **comparators**	**Relative** (95% CI)	**Absolute** (95% CI)		
Combined nutrition, physical activity, and psychological interventions vs any comparator (baseline to 12 months) – Meta-analysis												
1[a]	randomised trials	serious[b]	not serious	not serious	serious[c]	none	47	19	-	Hedges' g **0.25 lower** (0.74 lower to 0.23 higher)	⨁⨁◯◯ Low	Combined nutrition, physical activity, and psychological interventions may reduce adiposity slightly

CI: confidence interval

Explanations

a. 1 study, with 2 intervention arms
b. -1 using RoB-2 risk of bias rated Some concerns for all outcomes
c. -1 Imprecision due to 95% CI crosses 1 and small sample size (Total n<400)

Indigenous People

QUESTION

Should all interventions vs. treated/untreated comparators be used for weight maintenance/loss in Indigenous People experiencing overweight or obesity?	
POPULATION:	Weight maintenance/loss in Indigenous People experiencing overweight or obesity
INTERVENTION:	All interventions (any of the below singularly or in combination) • Nutrition • Physical activity • Sedentary behaviour • Psychological • Family-centred • Sleep • Pharmacological • Bariatric surgery
COMPARISON:	Treated/Untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	No conflicts of interest to declare.

ASSESSMENT

Problem Is the problem a priority?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Although no evidence was identified in Indigenous People, our review demonstrated a number of health risks associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y). **Children and adolescents (2 to <18y)** Blood pressure indicators Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9). Blood lipid profile Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol,	38% of Indigenous children and adolescents aged 2 to 17 years were living with overweight or obesity in 2018-19, which is an increase from 31% in 2012-2013 (211). These estimates are higher than the 24% of non-Indigenous children and adolescents living with overweight or obesity in 2017-18. 74% of Indigenous adults aged 18 years and over were living with overweight or obesity in 2018-19, which is an increase from 69% in 2012-2013 (211). In 2018-19 Indigenous adults were more likely to be living with overweight and obesity than non-Indigenous adults (77% versus 66%) (211). 45% of Indigenous adults aged 18 years and over were living with obesity in 2018-19, which is an

	and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15). <u>Cancer</u> Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19). <u>Mental health</u>	increase from 40% in 2012-2013 (211). In 2018-19 Indigenous adults were more likely to be living with obesity than non-Indigenous adults (47% versus 31%) (211).

	Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22). <u>Health-related quality of life ratings</u> Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23). <u>Reproductive health</u> Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24). **Young and middle-aged adults (18 to <65y)** <u>Cardiovascular disease</u> Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (25-36). Cardiovascular disease mortality increased with increasing weight (35, 37-39). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (40, 41), including ischemic stroke (40), and haemorrhagic stroke (40). Risk was also elevated for coronary artery disease (42, 43). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (44). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (45). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (29, 46-48). <u>Blood glucose level</u>	

A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (49).

<u>Type 2 diabetes mellitus</u>

Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (33, 43, 50-65).

Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (29, 49, 66-69).

<u>Non-alcoholic fatty liver disease</u>

Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (70-75).

Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (76-78). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (76).

<u>Musculoskeletal conditions</u>

Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (79). Young to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (80).

<u>Cancer</u>

When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (81, 82), thyroid (82-88), and blood cancers such as; lympho-haematopoietic (89) and diffuse large B-cell lymphoma (90, 91), multiple myeloma (82, 91-93), Hodgkin and non-Hodgkin lymphoma (82, 91), and leukemia (94, 95) (obesity only (96)).

Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (65, 81, 82, 87, 93, 94, 97-102), gastroesophageal (103, 104), gastric (82, 87, 102, 105, 106), and stomach (65) cancers; and liver (65, 82, 87, 93, 104, 107-116), gallbladder (65, 82, 93, 94, 117-119), bile duct (120), pancreatic (65, 87, 93, 94, 104, 121-123), small intestinal (121), and colorectal (81, 82, 87, 93, 94, 104, 122, 124-141) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (65, 81, 82, 87, 93, 94, 104, 134, 142-146), and bladder (65, 82, 144, 145, 147-150)).

In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (94) cancers, and total cancer risk was associated with increasing adiposity (151). Increased BMI in adulthood (≥18y) was protective against lung cancer (81, 152, 153), and pre-menopausal breast cancer (81, 154). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (155). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (156).

Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (82, 104, 157-160) (premenopausal (87, 161, 162) or postmenopausal (134) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (163). Risk of other gynaecological cancers also increased, including endometrial (81, 82, 93, 94, 131, 134, 164-167), uterine (65), and cervical cancers (82) (weak association with obesity (168)), as well as breast cancer (87, 94, 104, 131, 134, 151, 168-180). There was a greater risk of total and breast cancer mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (44). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (144, 181, 182), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (81, 183), while risk increased for development of advanced prostate cancer (104, 145, 183, 184) and prostate cancer mortality (185).

<u>Mental health</u>
Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (186). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (187, 188), or depression (189, 190), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (186).

<u>Health-related quality of life ratings</u>
Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (191).

<u>Reproductive health</u>
Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (192). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (193). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (194-198).

	Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (199). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (200). **Older adults (≥65y)** <ins>Cardiovascular disease</ins> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (201). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (202). Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (203). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (203). <ins>Type 2 diabetes mellitus</ins> Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (204, 205). <ins>Musculoskeletal conditions</ins> Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (206, 207). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (208, 209). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (210). <ins>Cancer</ins> A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (154).	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No evidence was identified in this population.	

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No evidence was identified in this population.	In addition to intentional adiposity loss, some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss. When people who are living with overweight or obesity are participating in a lifestyle weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. Older adults may be at increased risk of developing sarcopenia whilst undergoing weight-loss treatment.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No evidence was identified in this population.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of Indigenous People living with overweight or obesity in relation to receiving any treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for any treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach) may not prioritise weight management.

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. While no evidence was identified for this population. The committee has reached a consensus decision that given interventions have some degree of benefit for children, adolescents, young and middle-aged adults, and older adults, the balance would probably favour the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. When considering a nutrition intervention in older adults living with overweight or obesity, clinicians will need to balance the potential benefit from improving diet quality (and hence improved food and nutrient intakes) versus the need for weight reduction. Healthy dietary approaches with no specific daily energy intake goal may therefore be chosen instead of an energy target diet for the above reasons in order to balance quality of life. Clinical judgement will also be required for older adults living with overweight or obesity to balance priorities for health care in the presence of multiple co-morbidities that have their own nutrition recommendations (e.g. chronic kidney disease, insulin-requiring Diabetes, cancer, etc.) as well as age-related conditions (e.g. sarcopenia, osteoporosis/osteopenia, etc.) and treatment with medications that have weight or nutrition requirement implications.

Resources required

How large are the resource requirements (costs)?"

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ● Don't know	We have not sourced literature on the resources required for this intervention. Weight management interventions are not necessarily widely available and affordable.	This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it (212).

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of any intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact	We have not sourced literature about how health equity would be addressed through delivery of any intervention.	Social and health factors are interconnected and complex, with people from First Nations or

○ Probably increased ○ Increased ● Varies ○ Don't know		culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available programs; or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving any treatment. However, the committee believes any intervention is likely to be acceptable to the majority of people living with overweight or obesity and clinicians.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of any interventions in this population was not sourced.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			**No included studies**
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	**Don't know**
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	**Varies**	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Consensus statement due to limited evidence:

Indigenous People have continuously cared for the land and seas of Australia and are the longest living culture on Earth spanning 65,000 years. Since Colonisation there have been challenges emerge with Indigenous People's health and wellbeing, and voices of the community need to be valued and respected when applying the Guidelines in this group. There are challenges of affordability and access to healthy food and water, and food security exist. Access and affordability to culturally responsive health services including pharmacological and surgical interventions. A systems-wide approach to addressing social determinants of health is needed, for example, education, employment, housing, infrastructure, and early childhood education and care.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067

16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1
17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
26. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
27. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
28. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
29. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
30. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
31. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
32. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
33. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
34. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
35. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
36. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
37. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004

38. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247
39. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
40. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
41. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
42. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
43. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
44. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
45. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
46. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
47. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
48. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
49. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
50. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
51. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
52. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
53. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
54. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
55. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
56. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
57. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
58. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623

59. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129
60. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
61. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
62. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
63. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
64. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
65. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
66. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
67. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
68. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
69. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
70. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
71. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
72. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
73. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
74. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
75. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
76. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
77. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
78. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
79. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
80. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
81. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
82. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
83. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035

84. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177
85. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
86. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
87. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
88. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
89. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
90. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
91. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
92. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
93. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
94. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
95. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
96. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
97. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
98. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
99. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
100. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
101. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
102. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
103. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
104. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
105. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
106. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042

107. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602
108. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
109. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
110. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
111. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
112. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
113. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
114. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
115. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
116. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
117. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
118. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
119. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
120. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
121. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
122. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
123. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
124. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
125. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
126. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
127. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
128. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
129. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
130. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
131. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1

132. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
133. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
134. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
135. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
136. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
137. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
138. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
139. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
140. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
141. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
142. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
143. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
144. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
145. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
146. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
147. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
148. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
149. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
150. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
151. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
152. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
153. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
154. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
155. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037

156. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
157. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
158. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
159. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
160. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
161. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
162. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
163. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
164. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
165. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
166. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
167. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
168. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
169. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
170. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
171. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
172. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
173. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
174. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
175. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
176. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
177. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
178. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
179. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987

180. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
181. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
182. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
183. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
184. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
185. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
186. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
187. Ul‐Haq Z, Mackay DF, Fenwick E, Pell JP. Meta‐analysis of the association between body mass index and health‐related quality of life among adults, assessed by the SF‐36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
188. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
189. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
190. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence‐based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
191. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
192. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
193. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
194. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
195. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
196. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
197. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
198. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
199. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
200. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
201. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
202. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952

203. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002
204. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
205. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
206. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
207. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
208. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
209. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
210. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
211. Australian Institute of Health and Welfare. Overweight and obesity [Internet] Canberra: AIHW; 2024 [cited 2024 August 13]. Available from: https://www.aihw.gov.au/reports/overweight-obesity/overweight-and-obesity.
212. Australian Institute of Health and Welfare. Aboriginal and Torres Strait Islander Health Performance Framework: summary report August 2024.: Australian Government.; 2024 [cited 2024 August 26th]. Available from: https://www.indigenoushpf.gov.au/getattachment/79e5f9c5-f5b9-4a1f-8df6-187f267f6817/hpf_summary-report-aug-2024.pdf.

People from culturally and linguistically diverse backgrounds

QUESTION

Should all interventions vs. treated/untreated comparators be used for weight maintenance/loss in people from culturally and linguistically diverse backgrounds experiencing overweight or obesity?	
POPULATION:	Weight maintenance/loss in people from culturally and linguistically diverse backgrounds experiencing overweight or obesity
INTERVENTION:	All interventions (any of the below singularly or in combination) • Nutrition • Physical activity • Sedentary behaviour • Psychological • Family-centred • Sleep • Pharmacological • Bariatric surgery
COMPARISON:	Treated/Untreated comparators
MAIN OUTCOMES:	Weight loss or weight maintenance
CONFLICT OF INTERESTS:	Nil to declare

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Although no evidence was identified in people from a culturally and linguistically diverse background, our review demonstrated a number of health risks associated with overweight and obesity in a range of age groups, including children and adolescents (2 to <18y), young to middle-aged adults (18y to <65y), and older adults (≥65y). **Children and adolescents (2 to <18y)** <u>Blood pressure indicators</u> Prevalence of prehypertension (1), hypertension and elevated blood pressure (1-6) were significantly higher in children and adolescents with overweight or obesity, compared to those with a healthy weight. A systematic review of behavioural interventions aimed at treating overweight or obesity in children (5 to <12y) and adolescents (12 to <18y) demonstrated a reduction in mean BMI-SDS significantly improved systolic blood pressure, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein (7). Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing hypertension in adulthood (8, 9).	People born in Australia were more likely to be overweight or obese than those who were born overseas (69.8% compared to 58.9%) (2022 data) (211). Australian immigrant men from North Africa/Middle East, and Oceania had higher BMI than Australian-born men, whereas those from Southern and Central Asia had lower BMI (2011 data) (212). Male immigrants living in Australia for ≥15 years had higher BMI than those who had resided in Australia <5 years (212). Female immigrants living in Australia for ≥15 years had higher levels of overweight/obesity

	<u>Blood lipid profile</u> Prevalence of dyslipidaemia was greater in children and adolescents living with obesity when compared to those with a healthy weight. Blood triglyceride concentrations, low-density lipoprotein cholesterol, and total cholesterol were all shown to be higher in children with overweight or obesity than those in children with a healthy weight; conversely, high-density lipoprotein cholesterol was lower in children living with overweight or obesity (1, 4-6). Adolescents living with overweight or obesity who took part in weight loss randomised controlled trials had increased high-density lipoprotein cholesterol after the intervention (7). <u>Cardiovascular disease</u> Reviews of longitudinal cohort studies showed that childhood and adolescent overweight or obesity was associated with an increased risk of morbidity (8, 10) and mortality (9, 10) from coronary heart disease in adulthood. Men who had experienced overweight during adolescence also had higher mortality from coronary heart disease and stroke in adulthood (9). <u>Blood glucose level</u> Elevated fasting plasma glucose was more prevalent among children and adolescents experiencing overweight or obesity compared to those with healthy weight (1, 5, 6). When compared with children and adolescents of a healthy weight, insulin and insulin resistance levels were significantly greater among children and adolescents with obesity (5, 6). <u>Type 2 diabetes mellitus</u> Reviews of longitudinal cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence was associated with an increased risk of developing Type 2 diabetes mellitus in adulthood (8-10). <u>Non-alcoholic fatty liver disease</u> Reviews of prospective cohort studies increased biomarker indicators of non-alcoholic fatty liver disease (5) and risk of developing non-alcoholic fatty liver disease (1, 11-13) were prevalent among children and adolescents living with overweight or obesity. A systematic review examining randomised controlled trials that employed behavioural, nutrition, or pharmacological treatments for paediatric NAFLD in children and adolescents demonstrated that weight loss resulted in decreased biomarker indicators of non-alcoholic fatty liver disease (14). <u>Musculoskeletal conditions</u> Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood demonstrated that children and adolescents with overweight were more likely to experience musculoskeletal	than those who had resided in Australia <5 years (212). Immigrant men who arrived in Australia as children (0 to 11 years) or adolescents (12 to 17 years) had higher BMI and greater levels of overweight and obesity than those who arrived as adults (≥18 years) (212). Immigrant women who arrived in Australia as children had higher BMI and greater levels of overweight and obesity than those who arrived as adults (212).

pain, lower back pain, injuries, and fractures in adulthood when compared to those of a healthy weight (15).

Cancer

Reviews of observational cohort studies demonstrated that experiencing overweight or obesity during childhood and adolescence increased the risk of developing endometrial (16), and ovarian (16, 17) cancer during adulthood among women; and colorectal cancer (18) as an adult (men and women); with childhood obesity also associated with higher cancer mortality overall in adulthood (19).

Mental health

Reviews of observational studies showed that overweight and obesity in childhood and adolescence was associated with a greater risk of experiencing poorer psychological outcomes, including low self-esteem (5) and depression (5, 20) when compared to children and adolescents with a healthy weight. Reviews of observational cohort studies that tracked incidence of poor health from childhood to adulthood showed that children and adolescents experiencing obesity, particularly girls, had a significantly greater risk of developing depression, ongoing into adulthood, than children and adolescents with a healthy weight (21). Similarly, increasing weight gain from childhood to adulthood was associated with a higher risk of depression, especially in women (22).

Health-related quality of life ratings

Reviews of observational studies showed that living with overweight or obesity increased the risk of poorer health-related quality of life among children and adolescents (5). The risk of experiencing poorer health-related quality of life was also greater in adolescents with polycystic ovarian syndrome who were living with overweight or obesity compared with healthy-weight adolescents (23).

Reproductive health

Overweight and obesity during childhood and adolescence increased the risk of infertility in adulthood (24). Observational studies demonstrated that having obesity during adolescence was associated with having fewer children, nulliparity, and childlessness in adulthood (24). Childhood obesity led to greater risk of reproductive issues, such as menstrual/ovulatory problems and fertility problems in adult women, while men who had increased BMI during pre-puberty were more likely to have fewer sex-hormone binding globulin proteins (which can indirectly reduce fertility) than those who had healthy body weight during childhood (24).

Young and middle-aged adults (18 to <65y)

Cardiovascular disease

Cardiovascular disease risk was elevated in young and middle-aged adults living with overweight or obesity, when compared to those of a healthy weight (25-36). Cardiovascular disease mortality increased with increasing

	weight (35, 37-39). Reviews of cohort studies demonstrated that young to middle-aged adults living with overweight or obesity had an increased risk of stroke (40, 41), including ischemic stroke (40), and haemorrhagic stroke (40). Risk was also elevated for coronary artery disease (42, 43). Women surviving breast cancer who experienced obesity had an elevated risk of mortality from cardiovascular disease or 'other' causes, compared to healthy weight survivors (44). Reviews reporting on prospective cohort and case-control studies also showed that women with peripheral artery disease and overweight or obesity had increased risk of coronary heart disease and mortality from cardiovascular disease when compared to healthy weight adults (45). Reviews of randomised controlled trials aimed at reducing weight in young and middle-aged adults living with overweight or obesity demonstrated that with weight loss, participants' risk of mortality from cardiovascular disease decreased (29, 46-48). <u>Blood glucose level</u> A review of behaviour-based randomised controlled trial interventions aimed at Type 2 diabetes mellitus prevention showed that weight loss in young and middle-aged adults with overweight or obesity was associated with a reduction in fasting blood glucose levels (49). <u>Type 2 diabetes mellitus</u> Incidence of Type 2 diabetes mellitus was greater in young and middle-aged adults living with overweight or obesity compared to those with a healthy body weight, as demonstrated in reviews of cohort studies (33, 43, 50-65). Reviews of randomised controlled trials demonstrated that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity led to lower risk of Type 2 diabetes mellitus (29, 49, 66-69). <u>Non-alcoholic fatty liver disease</u> Prevalence of non-alcoholic fatty liver disease increased with increasing body weight (70-75). Reviews of randomised controlled trials showed that weight loss in young and middle-aged adults (aged 18-<65y) living with overweight or obesity resulted in a reduction in non-alcoholic fatty liver disease, including presence of non-alcoholic steatohepatitis (76-78). Weight-loss interventions employing behavioural, pharmacological, or surgical treatments resulted in lowering of liver biomarkers, and improved liver activity score (76). <u>Musculoskeletal conditions</u> Observational studies demonstrated that young and middle-aged adults living with overweight or obesity experienced a greater incidence of lower back and knee pain compared to adults with a healthy weight (79). Young	

	to middle-aged adults living with overweight or obesity had increased risk of musculoskeletal pain, disability, and complications post hip/knee arthroplasty versus their healthy-weight counterparts (80). <u>Cancer</u> When compared to healthy weight adults, those living with overweight and/or obesity had increased risk of morbidity and/or mortality from a range of cancers, including brain (81, 82), thyroid (82-88), and blood cancers such as; lympho-haematopoietic (89) and diffuse large B-cell lymphoma (90, 91), multiple myeloma (82, 91-93), Hodgkin and non-Hodgkin lymphoma (82, 91), and leukemia (94, 95) (obesity only (96)). Gastrointestinal system cancer risk was also increased among young and middle-aged adults living with overweight or obesity, including oesophageal adenocarcinoma (65, 81, 82, 87, 93, 94, 97-102), gastroesophageal (103, 104), gastric (82, 87, 102, 105, 106), and stomach (65) cancers; and liver (65, 82, 87, 93, 104, 107-116), gallbladder (65, 82, 93, 94, 117-119), bile duct (120), pancreatic (65, 87, 93, 94, 104, 121-123), small intestinal (121), and colorectal (81, 82, 87, 93, 94, 104, 122, 124-141) cancers. Overweight or obesity were also associated with greater risk of urinary cancers (kidney (65, 81, 82, 87, 93, 94, 104, 134, 142-146), and bladder (65, 82, 144, 145, 147-150)). In all adults (young and middle-aged adults, and older adults combined) risk of malignant melanoma (94) cancers, and total cancer risk was associated with increasing adiposity (151). Increased BMI in adulthood (≥18y) was protective against lung cancer (81, 152, 153), and pre-menopausal breast cancer (81, 154). In contrast, when waist circumference was used to indicate overweight or obesity, a positive association was found for increased central adiposity and lung cancer risk in adults (155). Having increased body weight (in young and middle-age and older adulthood combined) was also predictive of brain and central nervous system tumours, gliomas, and meningiomas (156). Longitudinal observational studies demonstrated increased risk of morbidity or mortality from gender-specific cancers among women and men living with overweight or obesity. When compared to women with healthy weight, women living with overweight or obesity were more likely to develop ovarian cancer (82, 104, 157-160) (premenopausal (87, 161, 162) or postmenopausal (134) ovarian cancer diagnosis). Women with overweight or obesity at the time of their ovarian cancer diagnosis had poorer survivability than women of a healthy body weight (163). Risk of other gynaecological cancers also increased, including endometrial (81, 82, 93, 94, 131, 134, 164-167), uterine (65), and cervical cancers (82) (weak association with obesity (168)), as well as breast cancer (87, 94, 104, 131, 134, 151, 168-180). There was a greater risk of total and breast cancer	

	mortality among adult women with overweight or obesity who were breast cancer survivors compared to healthy weight survivors (44). While some reviews showed that men were at greater risk of prostate-cancer related morbidity or mortality with increasing BMI (144, 181, 182), the relationship between BMI and prostate cancer incidence in men was less clear when stage of cancer was examined; there was a decreased risk for developing localized prostate cancer as BMI increased (81, 183), while risk increased for development of advanced prostate cancer (104, 145, 183, 184) and prostate cancer mortality (185). <u>Mental health</u> Young to middle-aged adults living with overweight or obesity had a greater risk of depression or symptoms of depression (186). Observational studies demonstrated poorer mental health in young and middle-aged adults experiencing overweight or obesity when compared to those with a healthy weight; e.g. physical and mental quality of life (187, 188), or depression (189, 190), including significant increases in depressive symptoms in patients living with obesity and Type 2 diabetes mellitus (186). <u>Health-related quality of life ratings</u> Health-related quality of life improved in young and middle-aged adults who lost weight when taking part in randomised controlled trials aimed at weight reduction (191). <u>Reproductive health</u> Longitudinal studies demonstrated that women experiencing overweight or obesity had a higher risk of miscarriage and lower rate of pregnancy and live birth post-IVF treatment compared to healthy weight women (192). Women who had polycystic ovary syndrome and a higher BMI experienced a higher rate of spontaneous abortion than those with a healthy body weight (193). Young and middle-aged men with overweight or obesity had increased risk of infertility when compared with men of a healthy body weight (194-198). Reviews of randomised controlled trials in young women living with overweight or obesity and diagnosed polycystic ovarian syndrome had improved reproductive outcomes including menstrual regularity and ovulation with weight loss (199). Similarly, weight loss after bariatric surgery treatment resulted in increased pregnancy rates in women (200). **Older adults (≥65y)** <u>Cardiovascular disease</u> The risk of cardiovascular events was associated with obesity in older adults with peripheral artery disease (201). Older adults with rheumatoid arthritis and obesity had a higher risk of cardiovascular morbidity compared to those with healthy weight status (202).	

	Conversely, among older adults who had atrial fibrillation, excess body weight was associated with protection against all-cause mortality (having obesity provided even greater protection) when compared with healthy body weight (203). Overweight or obesity (as indicated by BMI) in older adults who had atrial fibrillation was also associated with reduced risk of cardiovascular mortality when compared with older adults of a healthy BMI (203). Type 2 diabetes mellitus Overweight and obesity were associated with increased Type 2 diabetes mellitus incidence risk in older adults (204, 205). Musculoskeletal conditions Observational studies examining joint arthroplasty in older adults showed that those who underwent total hip arthroplasty who had a higher BMI had increased risk of musculoskeletal pain, complications and poor function pre- and post-surgery when compared with healthy weight adults (206, 207). Older adults with obesity undergoing total knee arthroplasty similarly experienced a higher risk of surgery revision, infection, and poorer knee function score post-surgery than their healthy-weight counterparts (208, 209). Observational studies also showed older adults living with overweight or obesity and knee osteoarthritis experienced lower health-related quality of life than healthy weight older adults with knee osteoarthritis (210). Cancer A review of prospective cohort studies found a higher risk of breast cancer in postmenopausal older women with overweight or obesity compared to healthy-weight older women (154).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No evidence was identified in this population.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	No evidence was identified in this population.	In addition to intentional adiposity loss, some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss. When people who are living with overweight or obesity are participating in a lifestyle weight loss intervention that incorporates diet change and increased physical activity, clinical judgement may be needed to balance priorities for health care in those who are vulnerable to disordered eating. Older adults may be at increased risk of developing sarcopenia whilst undergoing weight-loss treatment.

Certainty of evidence
What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No evidence was identified in this population.	

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	We have not sourced literature on the preferences and values of CALD people living with overweight or obesity in relation to receiving any treatment. However, the committee believes that since there are benefits, most people living with overweight or obesity would opt for any treatment.	Some people living with overweight or obesity (possibly including those guided by a weight neutral approach) may not prioritise weight management.

Balance of effects
Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ Don't know	Research evidence was drawn from desirable and undesirable effects, certainty of evidence and values above. The committee has reached a consensus decision that the balance between the desirable and undesirable effects favours the intervention.	While some people living with overweight or obesity may experience loss of lean mass (including bone density and muscle mass) during weight loss, overall, body composition improves due to greater loss of adiposity. When considering a nutrition intervention in older adults living with overweight or obesity, clinicians will need to balance the potential benefit from improving diet quality (and hence improved food and nutrient intakes) versus the need for weight reduction. Healthy dietary approaches with no specific daily energy intake goal may therefore be chosen instead of an energy target diet for the above reasons in order to balance quality of life. Clinical judgement will also be required for older adults living with overweight or obesity to balance priorities for health care in the presence of multiple co-morbidities that have their own nutrition recommendations (e.g. chronic kidney disease, insulin-requiring diabetes, cancer) as well as age-related conditions (e.g. sarcopenia, osteoporosis/osteopenia) and treatment with medications that have weight or nutrition requirement implications.
Resources required How large are the resource requirements (costs)?"		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**

○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know	We have not sourced literature on the resources required for this intervention. Weight management interventions are not necessarily widely available and affordable.	This treatment is likely to be cost effective but due to current resource constraints within the public health system, service access may be limited. Resources required will depend on setting, the intervention to be provided, and who provides it (213).

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	We have not assessed the certainty of evidence of required resources.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	No evidence on the cost effectiveness of any intervention was identified for this population.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ● Don't know	We have not sourced literature about how health equity would be addressed through delivery of any intervention.	Social and health factors are interconnected and complex, with people from First Nations or culturally and linguistically diverse groups, along with people living with a mental health condition or disability, and people living in

		regional or remote areas, having an increased likelihood of living with overweight or obesity. Access to weight management interventions may be unaffordable and/or inaccessible for these populations. Weight management interventions for these groups should be culturally sensitive, being developed and delivered with these communities. Equity could also be addressed by raising the patient's awareness of available treatments and avenues for access. For example, highlighting locally available programs, or when discussing the patient's care plan, practitioners should take into consideration whether the patient may face extended wait times or out-of-pocket expenses (i.e., gap payments) when accessing the prescribed treatment.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We have not sourced literature on the acceptability of receiving any treatment. However, the committee believes any intervention is likely to be acceptable to the majority of people living with overweight or obesity and clinicians.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Literature on the feasibility of any interventions in this population was not sourced.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			**No included studies**
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	**Varies**	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	**Don't know**
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation
Consensus statement due to limited evidence: We acknowledge and recognise the experiences of people from culturally and linguistically diverse backgrounds. Additional challenges may exist in interacting and engaging with the Australian health system. The voices of these individuals and their communities need to be valued and respected when applying the Guidelines. Improved access and affordability to culturally-responsive health services, including pharmacological and surgical interventions are needed for people living with overweight or obesity. A systems-wide approach to addressing social determinants of health is also necessary, for example education, employment, housing, infrastructure, and early childhood education and care. There may be variations in adiposity cut-points for some ethnicities, including Asian populations. Clinicians are encouraged to engage with translation services for patients for whom English is a second language.

REFERENCES SUMMARY

1. Sharma V, Coleman S, Nixon J, Sharples L, Hamilton-Shield J, Rutter H, Bryant M. A systematic review and meta-analysis estimating the population prevalence of comorbidities in children and adolescents aged 5 to 18 years. Obes Rev. 2019;20(10):1341-9. doi: 10.1111/obr.12904
2. Crouch SH, Soepnel LM, Kolkenbeck-Ruh A, Maposa I, Naidoo S, Davies J, et al. Paediatric hypertension in Africa: a systematic review and meta-analysis. EClinicalMedicine. 2022;43:101229. doi: 10.1016/j.eclinm.2021.101229
3. Noubiap JJ, Essouma M, Bigna JJ, Jingi AM, Aminde LN, Nansseu JR. Prevalence of elevated blood pressure in children and adolescents in Africa: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e375-e86. doi: 10.1016/S2468-2667(17)30123-8
4. Lichtenauer M, Wheatley SD, Martyn-St James M, Duncan MJ, Cobayashi F, Berg G, et al. Efficacy of anthropometric measures for identifying cardiovascular disease risk in adolescents: review and meta-analysis. Minerva Pediatr. 2018;70(4):371-82. doi: 10.23736/S0026-4946.18.05175-7
5. Sanders RH, Han A, Baker JS, Cobley S. Childhood obesity and its physical and psychological co-morbidities: a systematic review of Australian children and adolescents. Eur J Pediatr. 2015;174(6):715-46. doi: 10.1007/s00431-015-2551-3
6. Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM. Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and meta-analysis. BMJ. 2012;345:e4759. doi: 10.1136/bmj.e4759
7. El-Medany AYM, Birch L, Hunt LP, Matson RIB, Chong AHW, Beynon R, et al. What change in body mass index is required to improve cardiovascular outcomes in childhood and adolescent obesity through lifestyle interventions: a meta-regression. Child Obes. 2020;16(7):449-78. doi: 10.1089/chi.2019.0286
8. Llewellyn A, Simmonds M, Owen CG, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. Obes Rev. 2016;17(1):56-67. doi: 10.1111/obr.12316
9. Sommer A, Twig G. The impact of childhood and adolescent obesity on cardiovascular risk in adulthood: a systematic review. Curr Diabetes Rep. 2018;18(10):91. doi: 10.1007/s11892-018-1062-9
10. Park MH, Falconer C, Viner RM, Kinra S. The impact of childhood obesity on morbidity and mortality in adulthood: a systematic review. Obes Rev. 2012;13(11):985-1000. doi: 10.1111/j.1467-789X.2012.01015.x
11. Anderson EL, Howe LD, Jones HE, Higgins JPT, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS ONE. 2015;10(10):e0140908. doi: 10.1371/journal.pone.0140908
12. Zou Z-Y, Zeng J, Ren T-Y, Huang L-J, Wang M-Y, Shi Y-W, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: a systematic review and meta-analysis. Liver Int. 2022;42(9):1969-80. doi: 10.1111/liv.15080
13. Shalimar, Elhence A, Bansal B, Gupta H, Anand A, Singh TP, Goel A. Prevalence of non-alcoholic fatty liver disease in India: a systematic review and meta-analysis. J Clin Exp Hepatol. 2022;12(3):818-29. doi: 10.1016/j.jceh.2021.11.010
14. Mann JP, Tang GY, Nobili V, Armstrong MJ. Evaluations of lifestyle, dietary, and pharmacologic treatments for pediatric nonalcoholic fatty liver disease: a systematic review. Clin Gastroenterol Hepatol. 2019;17(8):1457-76.e7. doi: 10.1016/j.cgh.2018.05.023
15. Paulis WD, Silva S, Koes BW, van Middelkoop M. Overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15(1):52-67. doi: 10.1111/obr.12067
16. Byun D, Hong S, Ryu S, Nam Y, Jang H, Cho Y, et al. Early-life body mass index and risks of breast, endometrial, and ovarian cancers: a dose-response meta-analysis of prospective studies. Br J Canc. 2022;126(4):664-72. doi: 10.1038/s41416-021-01625-1

17. Ding N, Zhan J, Shi Y, Qiao T, Li P, Zhang T. Obesity in children and adolescents and the risk of ovarian cancer: a systematic review and dose-response meta-analysis. PLoS ONE. 2022. doi: 10.1371/journal.pone.0278050
18. Garcia H, Song M. Early-life obesity and adulthood colorectal cancer risk: a meta-analysis. Rev Panam Salud Publica. 2019;43:e3. doi: 10.26633/RPSP.2019.3
19. Mohammadian Khonsari N, Shahrestanaki E, Ehsani A, Asadi S, Sokoty L, Mohammadpoor Nami S, et al. Association of childhood and adolescence obesity with incidence and mortality of adulthood cancers. A systematic review and meta-analysis. Front Endocrinol. 2023;14:1069164. doi: 10.3389/fendo.2023.1069164
20. Godina-Flores NL, Gutierrez-Gómez YY, García-Botello M, López-Cruz L, Moreno-García CF, Aceves-Martins M. Obesity and its association with mental health among Mexican children and adolescents: systematic review. Nutr Rev. 2023;81(6):658–69. doi: 10.1093/nutrit/nuac083
21. Sutaria S, Devakumar D, Yasuda SS, Das S, Saxena S. Is obesity associated with depression in children? Systematic review and meta-analysis. Arch Dis Child. 2019;104(1):64-74. doi: 10.1136/archdischild-2017-314608
22. Gallagher C, Waidyatillake N, Pirkis J, Lambert K, Cassim R, Dharmage S, Erbas B. The effects of weight change from childhood to adulthood on depression and anxiety risk in adulthood: a systematic review. Obes Rev. 2023;24(7):e13566. doi: 10.1111/obr.13566
23. Kaczmarek C, Haller DM, Yaron M. Health-related quality of life in adolescents and young adults with polycystic ovary syndrome: a systematic review. J Pediatr Adolesc Gynecol. 2016;29(6):551-7. doi: 10.1016/j.jpag.2016.05.006
24. Pourghazi F, Eslami M, Mohammadi S, Ghoreshi R, Ejtahed H-S, Qorbani M. Association between childhood obesity and infertility in later life: a systematic review of cohort studies. BMC Endocr Disord. 2023;23:235. doi: 10.1186/s12902-023-01490-4
25. Huang M-Y, Wang M-Y, Lin Y-S, Lin C-J, Lo K, Chang I-J, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. Int J Environ Res Public Health. 2020;17(4). doi: 10.3390/ijerph17041320
26. Yeh T-L, Chen H-H, Tsai S-Y, Lin C-Y, Liu S-J, Chien K-L. The relationship between metabolically healthy obesity and the risk of cardiovascular disease: a systematic review and meta-analysis. J Clin Med. 2019;8(8). doi: 10.3390/jcm8081228
27. Fan J, Song Y, Chen Y, Hui R, Zhang W. Combined effect of obesity and cardio-metabolic abnormality on the risk of cardiovascular disease: a meta-analysis of prospective cohort studies. Int J Cardiol. 2013;168(5):4761-8. doi: 10.1016/j.ijcard.2013.07.230
28. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions?: a systematic review and meta-analysis. Ann Intern Med. 2013;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008
29. Zhang X, Zhu J, Kim JH, Sumerlin TS, Feng Q, Yu J. Metabolic health and adiposity transitions and risks of type 2 diabetes and cardiovascular diseases: a systematic review and meta-analysis. Diabetol Metab Syndr. 2023;15:50.
30. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J. 2021;42(34):3388-403. doi: 10.1093/eurheartj/ehab454
31. Mirzababaei A, Djafarian K, Mozafari H, Shab-Bidar S. The long-term prognosis of heart diseases for different metabolic phenotypes: a systematic review and meta-analysis of prospective cohort studies. Endocrine. 2019;63(3):439-62. doi: 10.1007/s12020-019-01840-0
32. Opio J, Croker E, Odongo GS, Attia J, Wynne K, McEvoy M. Metabolically healthy overweight/obesity are associated with increased risk of cardiovascular disease in adults, even in the absence of metabolic risk factors: a systematic review and meta-analysis of prospective cohort studies. Obes Rev. 2020;21(12):e13127. doi: 10.1111/obr.13127
33. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. Comput Biol Med. 2021;136:104754. doi: 10.1016/j.compbiomed.2021.104754
34. Xue R, Li Q, Geng Y, Wang H, Wang F, Zhang S. Abdominal obesity and risk of CVD: a dose-response meta-analysis of thirty-one prospective studies. Br J Nutr. 2021;126(9):1420-30. doi: 10.1017/S0007114521000064
35. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: a systematic review and dose-response meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2021;31(7):1976-84. doi: 10.1016/j.numecd.2021.03.003
36. Zheng R, Zhou D, Zhu Y. The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. J Epidemiol Community Health. 2016;70(10):1024-31. doi: 10.1136/jech-2015-206948
37. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. Prog Cardiovasc Dis. 2018;61(2):136-41. doi: 10.1016/j.pcad.2018.07.004
38. Kwon Y, Kim HJ, Park S, Park Y-G, Cho K-H. Body mass index-related mortality in patients with type 2 diabetes and heterogeneity in obesity paradox studies: a dose-response meta-analysis. PLoS ONE. 2017;12(1):e0168247. doi: 10.1371/journal.pone.0168247

39. Wang ZJ, Zhou YJ, Galper BZ, Gao F, Yeh RW, Mauri L. Association of body mass index with mortality and cardiovascular events for patients with coronary artery disease: a systematic review and meta-analysis. Heart. 2015;101(20):1631-8. doi: 10.1136/heartjnl-2014-307119
40. Guo Y, Yue X-J, Li H-H, Song Z-X, Yan H-Q, Zhang P, et al. Overweight and obesity in young adulthood and the risk of stroke: a meta-analysis. J Stroke Cerebrovasc Dis. 2016;25(12):2995-3004. doi: 10.1016/j.jstrokecerebrovasdis.2016.08.018
41. Yuan W, Wu B, Lou M, Song B, Han X, Sheng F, Xu W. Identification of risk factors for stroke in China: a meta-analysis of prospective cohort studies. Front Neurol. 2022;13:847304. doi: 10.3389/fneur.2022.847304
42. Mongraw-Chaffin ML, Peters SAE, Huxley RR, Woodward M. The sex-specific association between BMI and coronary heart disease: a systematic review and meta-analysis of 95 cohorts with 1.2 million participants. Lancet Diabetes Endocrinol. 2015;3(6):437-49. doi: 10.1016/S2213-8587(15)00086-8
43. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association between obesity and cardiovascular outcomes: a systematic review and meta-analysis of Mendelian randomization studies. JAMA Netw Open. 2018;1(7):e183788. doi: 10.1001/jamanetworkopen.2018.3788
44. Chan DSM, Vieira AR, Aune D, Bandera EV, Greenwood DC, McTiernan A, et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014;25(10):1901-14. doi: 10.1093/annonc/mdu042
45. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, et al. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018;33(9):831-45. doi: 10.1007/s10654-018-0374-z
46. Kane JA, Mehmood T, Munir I, Kamran H, Kariyanna PT, Zhyvotovska A, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019;4:131. doi: 10.15344/2456-8007/2019/131
47. Huang S, Shi K, Ren Y, Wang J, Yan W-F, Qian W-L, et al. Association of magnitude of weight loss and weight variability with mortality and major cardiovascular events among individuals with type 2 diabetes mellitus: a systematic review and meta-analysis. Cardiovasc Diabetol. 2022;21(1):78. doi: 10.1186/s12933-022-01503-x
48. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, Lopez-Jimenez F. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89(10):1368-77. doi: 10.1016/j.mayocp.2014.04.033
49. Galaviz KI, Weber MB, Straus A, Haw JS, Narayan KMV, Ali MK. Global diabetes prevention interventions: a systematic review and network meta-analysis of the real-world impact on incidence, weight, and glucose. Diabetes Care. 2018;41(7):1526-34. doi: 10.2337/dc17-2222
50. Kakoly NS, Khomami MB, Joham AE, Cooray SD, Misso ML, Norman RJ, et al. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Hum Reprod Update. 2018;24(4):455-67. doi: 10.1093/humupd/dmy007
51. Abdullah A, Peeters A, de Courten M, Stoelwinder J. The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. Diabetes Res Clin Pract. 2010;89(3):309-19. doi: 10.1016/j.diabres.2010.04.012
52. Bigna JJ, Nansseu JR, Katte J-C, Noubiap JJ. Prevalence of prediabetes and diabetes mellitus among adults residing in Cameroon: a systematic review and meta-analysis. Diabetes Res Clin Pract. 2018;137:109-18. doi: 10.1016/j.diabres.2017.12.005
53. Jayedi A, Soltani S, Motlagh SZ-T, Emadi A, Shahinfar H, Moosavi H, Shab-Bidar S. Anthropometric and adiposity indicators and risk of type 2 diabetes: systematic review and dose-response meta-analysis of cohort studies. BMJ. 2022;376:e067516. doi: 10.1136/bmj-2021-067516
54. Li H, Oldenburg B, Chamberlain C, O'Neil A, Xue B, Jolley D, et al. Diabetes prevalence and determinants in adults in China mainland from 2000 to 2010: a systematic review. Diabetes Res Clin Pract. 2012;98(2):226-35. doi: 10.1016/j.diabres.2012.05.010
55. Anagnostis P, Paparodis RD, Bosdou JK, Bothou C, Macut D, Goulis DG, Livadas S. Risk of type 2 diabetes mellitus in polycystic ovary syndrome is associated with obesity: a meta-analysis of observational studies. Endocrine. 2021;74(2):245-53. doi: 10.1007/s12020-021-02801-2
56. Babu GR, Murthy GVS, Ana Y, Patel P, Deepa R, Benjamin-Neelon SE, et al. Association of obesity with hypertension and type 2 diabetes mellitus in India: a meta-analysis of observational studies. World J Diabetes. 2018;9(1):40-52. doi: 10.4239/wjd.v9.i1.40
57. Cloostermans L, Wendel-Vos W, Doornbos G, Howard B, Craig CL, Kivimäki M, et al. Independent and combined effects of physical activity and body mass index on the development of type 2 diabetes—a meta-analysis of 9 prospective cohort studies. Int J Behav Nutr Phys Act. 2015;12:147. doi: 10.1186/s12966-015-0304-3
58. Kodama S, Fujihara K, Ishiguro H, Horikawa C, Ohara N, Yachi Y, et al. Unstable bodyweight and incident type 2 diabetes mellitus: a meta-analysis. J Diabetes Investig. 2017;8(4):501-9. doi: 10.1111/jdi.12623
59. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obes Rev. 2014;15(3):202-14. doi: 10.1111/obr.12129

60. Lotta LA, Abbasi A, Sharp SJ, Sahlqvist A-S, Waterworth D, Brosnan JM, et al. Definitions of metabolic health and risk of future type 2 diabetes in BMI categories: a systematic review and network meta-analysis. Diabetes Care. 2015;38(11):2177-87. doi: 10.2337/dc15-1218
61. Yu H-j, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Incidence and temporal trends in type 2 diabetes by weight status: a systematic review and meta-analysis of prospective cohort studies. J Glob Health. 2023;13:04088. doi: 10.7189/jogh.13.04088
62. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. Obes Rev. 2014;15(6):504-15. doi: 10.1111/obr.12157
63. Tajik S, Mirzababaei A, Ghaedi E, Kord-Varkaneh H, Mirzaei K. Risk of type 2 diabetes in metabolically healthy people in different categories of body mass index: an updated network meta-analysis of prospective cohort studies. J Cardiovasc Thorac Res. 2019;11(4):254-63. doi: 10.15171/jcvtr.2019.43
64. Yu H-J, Ho M, Liu X, Yang J, Chau PH, Fong DYT. Association of weight status and the risks of diabetes in adults: a systematic review and meta-analysis of prospective cohort studies. Int J Obes. 2022;46(6):1101-13. doi: 10.1038/s41366-022-01096-1
65. Larsson SC, Burgess S. Causal role of high body mass index in multiple chronic diseases: a systematic review and meta-analysis of Mendelian randomization studies. BMC Med. 2021;19(1):320. doi: 10.1186/s12916-021-02188-x
66. Merlotti C, Morabito A, Ceriani V, Pontiroli AE. Prevention of type 2 diabetes in obese at-risk subjects: a systematic review and meta-analysis. Acta Diabetol. 2014;51(5):853-63. doi: 10.1007/s00592-014-0624-9
67. Merlotti C, Morabito A, Pontiroli AE. Prevention of type 2 diabetes; a systematic review and meta-analysis of different intervention strategies. Diabetes Obes Metab. 2014;16(8):719-27. doi: 10.1111/dom.12270
68. Ricci C, Gaeta M, Rausa E, Asti E, Bandera F, Bonavina L. Long-term effects of bariatric surgery on type II diabetes, hypertension and hyperlipidemia: a meta-analysis and meta-regression study with 5-year follow-up. Obes Surg. 2015;25(3):397-405. doi: 10.1007/s11695-014-1442-4
69. Yan Y-x, Wang G-f, Xu N, Wang F-l. Correlation between postoperative weight loss and diabetes mellitus remission: a meta-analysis. Obes Surg. 2014;24(11):1862-9. doi: 10.1007/s11695-014-1285-z
70. Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, et al. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020;14(2):259-69. doi: 10.1007/s12072-020-10023-3
71. Im HJ, Ahn YC, Wang J-H, Lee MM, Son CG. Systematic review on the prevalence of nonalcoholic fatty liver disease in South Korea. Clin Res Hepatol Gastroenterol. 2021;45(4):101526. doi: 10.1016/j.clinre.2020.06.022
72. Pang Q, Zhang J-Y, Song S-D, Qu K, Xu X-S, Liu S-S, Liu C. Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. World J Gastroenterol. 2015;21(5):1650-62. doi: 10.3748/wjg.v21.i5.1650
73. Sookoian S, Pirola CJ. Systematic review with meta-analysis: the significance of histological disease severity in lean patients with nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2018;47(1):16-25. doi: 10.1111/apt.14401
74. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, Yasuda S, et al. Clinical profiles of Asians with NAFLD: a systematic review and meta-analysis. Dig Dis. 2022;40(6):734-44. doi: 10.1159/000521662
75. Wu J, Yao X-Y, Shi R-X, Liu S-F, Wang X-Y. A potential link between polycystic ovary syndrome and non-alcoholic fatty liver disease: an update meta-analysis. Reprod Health. 2018;15(1):77. doi: 10.1186/s12978-018-0519-2
76. Koutoukidis DA, Astbury NM, Tudor KE, Morris E, Henry JA, Noreik M, et al. Association of weight loss interventions with changes in biomarkers of nonalcoholic fatty liver disease: a systematic review and meta-analysis. JAMA Intern Med. 2019;179(7):1262-71. doi: 10.1001/jamainternmed.2019.2248
77. Panunzi S, Maltese S, Verrastro O, Labbate L, De Gaetano A, Pompili M, et al. Pioglitazone and bariatric surgery are the most effective treatments for non-alcoholic steatohepatitis: a hierarchical network meta-analysis. Diabetes Obes Metab. 2021;23(4):980-90. doi: 10.1111/dom.14304
78. Koutoukidis DA, Koshiaris C, Henry JA, Noreik M, Morris E, Manoharan I, et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: a systematic review and meta-analysis. Metabolism. 2021;115:154455. doi: 10.1016/j.metabol.2020.154455
79. Peiris WL, Cicuttini FM, Hussain SM, Estee MM, Romero L, Ranger TA, et al. Is adiposity associated with back and lower limb pain? A systematic review. PLoS ONE. 2021;16(9):e0256720. doi: 10.1371/journal.pone.0256720
80. Pozzobon D, Ferreira PH, Blyth FM, Machado GC, Ferreira ML. Can obesity and physical activity predict outcomes of elective knee or hip surgery due to osteoarthritis? A meta-analysis of cohort studies. BMJ Open. 2018;8(2):e017689. doi: 10.1136/bmjopen-2017-017689
81. Fang X, Wei J, He X, Lian J, Han D, An P, et al. Quantitative association between body mass index and the risk of cancer: a global meta-analysis of prospective cohort studies. Int J Cancer. 2018;143(7):1595-603. doi: 10.1002/ijc.31553
82. Chen J, Ke K, Liu Z, Yang L, Wang L, Zhou J, Dong Q. Body mass index and cancer risk: an umbrella review of meta-analyses of observational studies. Nutr Cancer. 2023;75(4). doi: 10.1080/01635581.2023.2180824
83. Ma J, Huang M, Wang L, Ye W, Tong Y, Wang H. Obesity and risk of thyroid cancer: evidence from a meta-analysis of 21 observational studies. Med Sci Monit. 2015;21:283-91. doi: 10.12659/MSM.892035
84. Peterson E, De P, Nuttall R. BMI, diet and female reproductive factors as risks for thyroid cancer: a systematic review. PLoS ONE. 2012;7(1):e29177. doi: 10.1371/journal.pone.0029177

85. Sadeghi H, Rafei M, Bahrami M, Haghdoost A, Shabani Y. Attributable risk fraction of four lifestyle risk factors of thyroid cancer: a meta-analysis. J Public Health (Oxf). 2018;40(2):e91-e8. doi: 10.1093/pubmed/fdx088
86. Schmid D, Ricci C, Behrens G, Leitzmann MF. Adiposity and risk of thyroid cancer: a systematic review and meta-analysis. Obes Rev. 2015;16(12):1042-54. doi: 10.1111/obr.12321
87. Wang J, Yang D-L, Chen Z-Z, Gou B-F. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol. 2016;42:1-8. doi: 10.1016/j.canep.2016.02.010
88. Youssef MR, Reisner ASC, Attia AS, Hussein MH, Omar M, LaRussa A, et al. Obesity and the prevention of thyroid cancer: impact of body mass index and weight change on developing thyroid cancer - pooled results of 24 million cohorts. Oral Oncol. 2021;112:105085. doi: 10.1016/j.oraloncology.2020.105085
89. Abar L, Sobiecki JG, Cariolou M, Nanu N, Vieira AR, Stevens C, et al. Body size and obesity during adulthood, and risk of lympho-haematopoietic cancers: an update of the WCRF-AICR systematic review of published prospective studies. Ann Oncol. 2019;30(4):528-41. doi: 10.1093/annonc/mdz045
90. Castillo JJ, Ingham RR, Reagan JL, Furman M, Dalia S, Mitri J. Obesity is associated with increased relative risk of diffuse large B-cell lymphoma: a meta-analysis of observational studies. Clin Lymphoma Myeloma Leuk. 2014;14(2):122-30. doi: 10.1016/j.clml.2013.10.005
91. Psaltopoulou T, Sergentanis TN, Ntanasis-Stathopoulos I, Tzanninis I-G, Riza E, Dimopoulos MA. Anthropometric characteristics, physical activity and risk of hematological malignancies: a systematic review and meta-analysis of cohort studies. Int J Cancer. 2019;145(2):347-59. doi: 10.1002/ijc.32109
92. Wallin A, Larsson SC. Body mass index and risk of multiple myeloma: a meta-analysis of prospective studies. Eur J Cancer. 2011;47(11):1606-15. doi: 10.1016/j.ejca.2011.01.020
93. Kyrgiou M, Kalliala I, Markozannes G, Gunter MJ, Paraskevaidis E, Gabra H, et al. Adiposity and cancer at major anatomical sites: umbrella review of the literature. BMJ. 2017;356:j477. doi: 10.1136/bmj.j477
94. Dobbins M, Decorby K, Choi BCK. The association between obesity and cancer risk: a meta-analysis of observational studies from 1985 to 2011. ISRN Prev Med. 2013;2013:680536. doi: 10.5402/2013/680536
95. Li S, Chen L, Jin W, Ma X, Ma Y, Dong F, et al. Influence of body mass index on incidence and prognosis of acute myeloid leukemia and acute promyelocytic leukemia: a meta-analysis. Sci Rep. 2017;7(1):17998. doi: 10.1038/s41598-017-18278-x
96. Castillo JJ, Reagan JL, Ingham RR, Furman M, Dalia S, Merhi B, et al. Obesity but not overweight increases the incidence and mortality of leukemia in adults: a meta-analysis of prospective cohort studies. Leuk Res. 2012;36(7):868-75. doi: 10.1016/j.leukres.2011.12.020
97. Vingeliene S, Chan DSM, Vieira AR, Polemiti E, Stevens C, Abar L, et al. An update of the WCRF/AICR systematic literature review and meta-analysis on dietary and anthropometric factors and esophageal cancer risk. Ann Oncol. 2017;28(10):2409-19. doi: 10.1093/annonc/mdx338
98. Castro C, Peleteiro B, Lunet N. Modifiable factors and esophageal cancer: a systematic review of published meta-analyses. J Gastroenterol. 2018;53:37-51. doi: 10.1007/s00535-017-1375-5
99. Nucci D, Marino A, Realdon S, Nardi M, Fatigoni C, Gianfredi V. Lifestyle, WCRF/AICR recommendations, and esophageal adenocarcinoma risk: a systematic review of the literature. Nutrients. 2021;13(10). doi: 10.3390/nu13103525
100. Singh S, Sharma AN, Murad MH, Buttar NS, El-Serag HB, Katzka DA, Iyer PG. Central adiposity is associated with increased risk of esophageal inflammation, metaplasia, and adenocarcinoma: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(11):1399-412.e7. doi: 10.1016/j.cgh.2013.05.009
101. Tian J, Zuo C, Liu G, Che P, Li G, Li X, Chen H. Cumulative evidence for the relationship between body mass index and the risk of esophageal cancer: an updated meta-analysis with evidence from 25 observational studies. J Gastroenterol Hepatol. 2020;35(5):730-43. doi: 10.1111/jgh.14917
102. Turati F, Tramacere I, La Vecchia C, Negri E. A meta-analysis of body mass index and esophageal and gastric cardia adenocarcinoma. Ann Oncol. 2013;24(3):609-17. doi: 10.1093/annonc/mds244
103. Du X, Hidayat K, Shi B-M. Abdominal obesity and gastroesophageal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(3):BSR20160474. doi: 10.1042/BSR20160474
104. Shanmugalingam T, Crawley D, Bosco C, Melvin J, Rohrmann S, Chowdhury S, et al. Obesity and cancer: the role of vitamin D. BMC Cancer. 2014;14:712. doi: 10.1186/1471-2407-14-712
105. Azizi N, Zangiabadian M, Seifi G, Davari A, Yekekhani E, Safavi-Naini SAA, et al. Gastric cancer risk in association with underweight, overweight, and obesity: a systematic review and meta-analysis. Cancers (Basel). 2023;15(10):2778. doi: 10.3390/cancers15102778
106. Chen Y, Liu L, Wang X, Wang J, Yan Z, Cheng J, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. Cancer Epidemiol Biomarkers Prev. 2013;22(8):1395-408. doi: 10.1158/1055-9965.EPI-13-0042
107. Yang C, Lu Y, Xia H, Liu H, Pan D, Yang X, Sun G. Excess body weight and the risk of liver cancer: systematic review and a meta-analysis of cohort studies. Nutr Cancer. 2020;72(7):1085-97. doi: 10.1080/01635581.2019.1664602

108. Saunders D, Seidel D, Allison M, Lyratzopoulos G. Systematic review: the association between obesity and hepatocellular carcinoma - epidemiological evidence. Aliment Pharmacol Ther. 2010;31(10):1051-63. doi: 10.1111/j.1365-2036.2010.04271.x
109. Rui R, Lou J, Zou L, Zhong R, Wang J, Xia D, et al. Excess body mass index and risk of liver cancer: a nonlinear dose-response meta-analysis of prospective studies. PLoS ONE. 2012;7(9):e44522. doi: 10.1371/journal.pone.0044522
110. Sohn W, Lee HW, Lee S, Lim JH, Lee MW, Park CH, Yoon SK. Obesity and the risk of primary liver cancer: a systematic review and meta-analysis. Clin Mol Hepatol. 2021;27(1):157-74. doi: 10.3350/cmh.2020.0176
111. Tanaka K, Tsuji I, Tamakoshi A, Matsuo K, Ito H, Wakai K, et al. Obesity and liver cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2012;42(3):212-21. doi: 10.1093/jjco/hyr198
112. Yan L-J, Yang L-S, Yan Y-C, Tan S-Y, Ding Z-N, Liu H, et al. Anthropometric indicators of adiposity and risk of primary liver cancer: a systematic review and dose-response meta-analysis. Eur J Cancer. 2023;185:150-63. doi: 10.1016/j.ejca.2023.03.005
113. Yang L-S, Yan L-J, Yan Y-C, Ding Z-N, Liu H, Tan S-Y, et al. Regional and sex differences in the mortality risk associated with primary liver cancer in obesity: a systematic review and meta-analysis. Nutrition. 2023;113:112097. doi: 10.1016/j.nut.2023.112097
114. Chen J, Song S, Li X, Bian D, Wu X. Association of metabolic traits with occurrence of nonalcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis of longitudinal cohort studies. Saudi J Gastroenterol. 2022;28(2):92-100. doi: 10.4103/sjg.sjg_260_21
115. Gupta A, Das A, Majumder K, Arora N, Mayo HG, Singh PP, et al. Obesity is independently associated with increased risk of hepatocellular cancer-related mortality: a systematic review and meta-analysis. Am J Clin Oncol. 2018;41(9):874-81. doi: 10.1097/COC.0000000000000388
116. Liu X, Ju W, Huo C, Zhang S, Wang X, Huang K. Overweight and obesity as independent factors for increased risk of hepatocellular cancer-related mortality: a meta-analysis. J Am Coll Nutr. 2021;40(3):287-93. doi: 10.1080/07315724.2020.1751007
117. Li L, Gan Y, Li W, Wu C, Lu Z. Overweight, obesity and the risk of gallbladder and extrahepatic bile duct cancers: a meta-analysis of observational studies. Obesity. 2016;24(8):1786-802. doi: 10.1002/oby.21505
118. Tan W, Gao M, Liu N, Zhang G, Xu T, Cui W. Body mass index and risk of gallbladder cancer: systematic review and meta-analysis of observational studies. Nutrients. 2015;7(10):8321-234. doi: 10.3390/nu7105387
119. Liu H, Zhang Y, Ai M, Wang J, Jin B, Teng Z, et al. Body mass index can increase the risk of gallbladder cancer: a meta-analysis of 14 cohort studies. Med Sci Monit Basic Res. 2016;22:146-55. doi: 10.12659/msmbr.901651
120. Li J-S, Han T-J, Jing N, Li L, Zhang X-H, Ma F-Z, Liu J-Y. Obesity and the risk of cholangiocarcinoma: a meta-analysis. Tumour Biol. 2014;35(7):6831-8. doi: 10.1007/s13277-014-1939-4
121. Leoncini E, Carioli G, La Vecchia C, Boccia S, Rindi G. Risk factors for neuroendocrine neoplasms: a systematic review and meta-analysis. Ann Oncol. 2016;27(1):68-81. doi: 10.1093/annonc/mdv505
122. Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H. Obesity and risk of colorectal cancer: a systematic review of prospective studies. PLoS ONE. 2013;8(1):e53916. doi: 10.1371/journal.pone.0053916
123. Aune D, Greenwood DC, Chan DSM, Vieira R, Vieira AR, Navarro Rosenblatt DA, et al. Body mass index, abdominal fatness and pancreatic cancer risk: a systematic review and non-linear dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(4):843-52. doi: 10.1093/annonc/mdr398
124. Kokts-Porietis RL, Elmrayed S, Brenner DR, Friedenreich CM. Obesity and mortality among endometrial cancer survivors: a systematic review and meta-analysis. Obes Rev. 2021;22(12):e13337. doi: 10.1111/obr.13337
125. Zhang C, Cheng Y, Luo D, Wang J, Liu J, Luo Y, et al. Association between cardiovascular risk factors and colorectal cancer: a systematic review and meta-analysis of prospective cohort studies. EClinicalMedicine. 2021;34:100794. doi: 10.1016/j.eclinm.2021.100794
126. Abar L, Vieira AR, Aune D, Sobiecki JG, Vingeliene S, Polemiti E, et al. Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies. Eur J Nutr. 2018;57(5):1701-20. doi: 10.1007/s00394-017-1557-1
127. Chen Q, Wang J, Yang J, Jin Z, Shi W, Qin Y, et al. Association between adult weight gain and colorectal cancer: a dose-response meta-analysis of observational studies. Int J Cancer. 2015;136(12):2880-9. doi: 10.1002/ijc.29331
128. O'Sullivan DE, Sutherland RL, Town S, Chow K, Fan J, Forbes N, et al. Risk factors for early-onset colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2022;20(6):1229-40.e5. doi: 10.1016/j.cgh.2021.01.037
129. Jaspan V, Lin K, Popov V. The impact of anthropometric parameters on colorectal cancer prognosis: a systematic review and meta-analysis. Crit Rev Oncol Hematol. 2021;159:103232. doi: 10.1016/j.critrevonc.2021.103232
130. Dong Y, Zhou J, Zhu Y, Luo L, He T, Hu H, et al. Abdominal obesity and colorectal cancer risk: systematic review and meta-analysis of prospective studies. Biosci Rep. 2017;37(6):BSR20170945. doi: 10.1042/BSR20170945
131. Druesne-Pecollo N, Touvier M, Barrandon E, Chan DSM, Norat T, Zelek L, et al. Excess body weight and second primary cancer risk after breast cancer: a systematic review and meta-analysis of prospective studies. Breast Cancer Res Treat. 2012;135(3):647-54. doi: 10.1007/s10549-012-2187-1

132. Fardet A, Druesne-Pecollo N, Touvier M, Latino-Martel P. Do alcoholic beverages, obesity and other nutritional factors modify the risk of familial colorectal cancer? A systematic review. Crit Rev Oncol Hematol. 2017;119:94-112. doi: 10.1016/j.critrevonc.2017.09.001
133. Goodarzi G, Mozaffari H, Raeisi T, Mehravar F, Razi B, Ghazi ML, et al. Metabolic phenotypes and risk of colorectal cancer: a systematic review and meta-analysis of cohort studies. BMC Cancer. 2022;22:89. doi: 10.1186/s12885-021-09149-w
134. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. J Natl Cancer Inst. 2015;107(2):djv088. doi: 10.1093/jnci/djv088
135. Lee J, Meyerhardt JA, Giovannucci E, Jeon JY. Association between body mass index and prognosis of colorectal cancer: a meta-analysis of prospective cohort studies. PLoS ONE. 2015;10(3):e0120706. doi: 10.1371/journal.pone.0120706
136. Lei X, Song S, Li X, Geng C, Wang C. Excessive body fat at a young age increases the risk of colorectal cancer: a systematic review and meta-analysis. Nutr Cancer. 2021;73(9):1601-12. doi: 10.1080/01635581.2020.1804951
137. Li H, Boakye D, Chen X, Hoffmeister M, Brenner H. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol. 2021;116(11):2173-83. doi: 10.14309/ajg.0000000000001393
138. Zhang R, Boakye D, Yang N, Zhou X, Zhou Y, Jiang F, et al. Field synopsis of environmental and genetic risk factors of sporadic early-onset colorectal cancer and advanced adenoma. Cancer Epidemiol Biomarkers Prev. 2023;32(8):1048–60. doi: 10.1158/1055-9965.EPI-22-1316
139. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. Eur J Cancer Prev. 2013;22(6):492-505. doi: 10.1097/CEJ.0b013e328360f434
140. Deng Y, Wang L, Huang J, Ding H, Wong MCS. Associations between potential causal factors and colorectal cancer risk: a systematic review and meta-analysis of Mendelian randomization studies. J Dig Dis. 2022;23(8-9):435-45. doi: 10.1111/1751-2980.13130
141. Mandic M, Li H, Safizadeh F, Niedermaier T, Hoffmeister M, Brenner H. Is the association of overweight and obesity with colorectal cancer underestimated? An umbrella review of systematic reviews and meta-analyses. Eur J Epidemiol. 2023;38:135–44. doi: 10.1007/s10654-022-00954-6
142. Liu X, Sun Q, Hou H, Zhu K, Wang Q, Liu H, et al. The association between BMI and kidney cancer risk: an updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine. 2018;97(44):e12860. doi: 10.1097/MD.0000000000012860
143. Golabek T, Bukowczan J, Szopinski T, Chlosta P, Lipczynski W, Dobruch J, Borowka A. Obesity and renal cancer incidence and mortality--a systematic review of prospective cohort studies. Ann Agric Environ Med. 2016;23(1):37-43. doi: 10.5604/12321966.1196850
144. Shi J, Zhao L, Gao Y, Niu M, Yan M, Chen Y, et al. Associating the risk of three urinary cancers with obesity and overweight: an overview with evidence mapping of systematic reviews. Syst Rev. 2021;10(1):58. doi: 10.1186/s13643-021-01606-8
145. Papavasileiou G, Tsilingiris D, Spyrou N, Vallianou NG, Karampela I, Magkos F, Dalamaga M. Obesity and main urologic cancers: current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70-98. doi: 10.1016/j.semcancer.2023.03.002
146. Al-Bayati O, Hasan A, Pruthi D, Kaushik D, Liss MA. Systematic review of modifiable risk factors for kidney cancer. Urol Oncol. 2019;37(6):359-71. doi: 10.1016/j.urolonc.2018.12.008
147. Qin Q, Xu X, Wang X, Zheng X-Y. Obesity and risk of bladder cancer: a meta-analysis of cohort studies. Asian Pac J Cancer Prev. 2013;14(5):3117-21. doi: 10.7314/APJCP.2013.14.5.3117
148. Sun J-W, Zhao L-G, Yang Y, Ma X, Wang Y-Y, Xiang Y-B. Obesity and risk of bladder cancer: a dose-response meta-analysis of 15 cohort studies. PLoS ONE. 2015;10(3):e0119313. doi: 10.1371/journal.pone.0119313
149. Tzelves L, Xenou D, Skolarikos A, Varkarakis I, Deliveliotis C, Terpos E, et al. Association of obesity and other anthropometric characteristics with bladder cancer risk: a systematic review and meta-analysis of longitudinal cohort studies. J BUON. 2021;26(3):1040-55.
150. Zhao L, Tian X, Duan X, Ye Y, Sun M, Huang J. Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. Oncotarget. 2017;8(20):33990-4000. doi: 10.18632/oncotarget.16722
151. Soltani S, Abdollahi S, Aune D, Jayedi A. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. Sci Rep. 2021;11(1):2479. doi: 10.1038/s41598-021-81671-0
152. Duan P, Hu C, Quan C, Yi X, Zhou W, Yuan M, et al. Body mass index and risk of lung cancer: systematic review and dose-response meta-analysis. Sci Rep. 2015;5:16938. doi: 10.1038/srep16938
153. Gupta A, Majumder K, Arora N, Mayo HG, Singh PP, Beg MS, et al. Premorbid body mass index and mortality in patients with lung cancer: a systematic review and meta-analysis. Lung Cancer. 2016;102:49-59. doi: 10.1016/j.lungcan.2016.10.017
154. Chen Y, Liu L, Zhou Q, Imam MU, Cai J, Wang Y, et al. Body mass index had different effects on premenopausal and postmenopausal breast cancer risks: a dose-response meta-analysis with 3,318,796 subjects from 31 cohort studies. BMC Public Health. 2017;17(1):936. doi: 10.1186/s12889-017-4953-9
155. Gao J, Lin X, He Y, Fu Y, Wu Y, Liao J, et al. The comparison of different obesity indexes and the risk of lung cancer: a meta-analysis of prospective cohort studies. Nutr Cancer. 2019;71(6):908-21. doi: 10.1080/01635581.2019.1595037

156. Sergentanis TN, Tsivgoulis G, Perlepe C, Ntanasis-Stathopoulos I, Tzanninis I-G, Sergentanis IN, Psaltopoulou T. Obesity and risk for brain/CNS tumors, gliomas and meningiomas: a meta-analysis. PLoS ONE. 2015;10(9):e0136974. doi: 10.1371/journal.pone.0136974
157. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. Asian Pac J Cancer Prev. 2014;15(18):7665-71. doi: 10.7314/APJCP.2014.15.18.7665
158. Yang H-S, Yoon C, Myung S-K, Park SM. Effect of obesity on survival of women with epithelial ovarian cancer: a systematic review and meta-analysis of observational studies. Int J Gynecol Cancer. 2011;21(9):1525-32. doi: 10.1097/IGC.0b013e31822eb5f8
159. Aune D, Navarro Rosenblatt DA, Chan DSM, Abar L, Vingeliene S, Vieira AR, et al. Anthropometric factors and ovarian cancer risk: a systematic review and nonlinear dose-response meta-analysis of prospective studies. Int J Cancer. 2015;136(8):1888-98. doi: 10.1002/ijc.29207
160. Foong KW, Bolton H. Obesity and ovarian cancer risk: a systematic review. Post Reprod Health. 2017;23(4):183-98. doi: 10.1177/2053369117709225
161. Ellwanger B, Schüler-Toprak S, Jochem C, Leitzmann MF, Baurecht H. Anthropometric factors and the risk of ovarian cancer: a systematic review and meta-analysis. Cancer Rep (Hoboken). 2022;5(11):e1618. doi: 10.1002/cnr2.1618
162. Liu Z, Zhang T-T, Zhao J-J, Qi S-F, Du P, Liu D-W, Tian Q-B. The association between overweight, obesity and ovarian cancer: a meta-analysis. Jpn J Clin Oncol. 2015;45(12):1107-15. doi: 10.1093/jjco/hyv150
163. Bae HS, Kim HJ, Hong JH, Lee JK, Lee NW, Song JY. Obesity and epithelial ovarian cancer survival: a systematic review and meta-analysis. J Ovarian Res. 2014;7:41. doi: 10.1186/1757-2215-7-41
164. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health. 2015;129(7):872-80. doi: 10.1016/j.puhe.2015.04.017
165. Esposito K, Chiodini P, Capuano A, Bellastella G, Maiorino MI, Giugliano D. Metabolic syndrome and endometrial cancer: a meta-analysis. Endocrine. 2014;45:28-36. doi: 10.1007/s12020-013-9973-3
166. Wise MR, Jordan V, Lagas A, Showell M, Wong N, Lensen S, Farquhar CM. Obesity and endometrial hyperplasia and cancer in premenopausal women: a systematic review. Am J Obstet Gynecol. 2016;214(6):689.e1-.e17. doi: 10.1016/j.ajog.2016.01.175
167. Zhang Y, Liu H, Yang S, Zhang J, Qian L, Chen X. Overweight, obesity and endometrial cancer risk: results from a systematic review and meta-analysis. Int J Biol Markers. 2014;29(1):e21-e9. doi: 10.5301/jbm.5000047
168. Poorolajal J, Jenabi E. The association between BMI and cervical cancer risk: a meta-analysis. Eur J Cancer Prev. 2016;25(3):232-8. doi: 10.1097/CEJ.0000000000000164
169. Namiranian N, Moradi-Lakeh M, Razavi-Ratki SK, Doayie M, Nojomi M. Risk factors of breast cancer in the Eastern Mediterranean Region: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(21):9535-41. doi: 10.7314/APJCP.2014.15.21.9535
170. Akdeniz D, Klaver MM, Smith CZA, Koppert LB, Hooning MJ. The impact of lifestyle and reproductive factors on the risk of a second new primary cancer in the contralateral breast: a systematic review and meta-analysis. Cancer Causes Control. 2020;31(5):403-16. doi: 10.1007/s10552-020-01284-2
171. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013;137(1):307-14. doi: 10.1007/s10549-012-2339-3
172. Amadou A, Ferrari P, Muwonge R, Moskal A, Biessy C, Romieu I, Hainaut P. Overweight, obesity and risk of premenopausal breast cancer according to ethnicity: a systematic review and dose-response meta-analysis. Obes Rev. 2013;14(8):665-78. doi: 10.1111/obr.12028
173. Khoramdad M, Solaymani-Dodaran M, Kabir A, Ghahremanzadeh N, Hashemi E-o-S, Fahimfar N, et al. Breast cancer risk factors in Iranian women: a systematic review and meta-analysis of matched case-control studies. Eur J Med Res. 2022;27:311. doi: 10.1186/s40001-022-00952-0
174. Namazi N, Irandoost P, Heshmati J, Larijani B, Azadbakht L. The association between fat mass and the risk of breast cancer: a systematic review and meta-analysis. Clin Nutr. 2019;38(4):1496-503. doi: 10.1016/j.clnu.2018.09.013
175. Parekh N, Chandran U, Bandera EV. Obesity in cancer survival. Annu Rev Nutr. 2012;32:311-42. doi: 10.1146/annurev-nutr-071811-150713
176. Xia X, Chen W, Li J, Chen X, Rui R, Liu C, et al. Body mass index and risk of breast cancer: a nonlinear dose-response meta-analysis of prospective studies. Sci Rep. 2014;4:7480. doi: 10.1038/srep07480
177. Zahedi R, Molavi Vardanjani H, Baneshi MR, Haghdoost AA, Malekpour Afshar R, Ershad Sarabi R, et al. Incidence trend of breast cancer in women of eastern Mediterranean region countries from 1998 to 2019: a systematic review and meta-analysis. BMC Womens Health. 2020;20(1):53. doi: 10.1186/s12905-020-00903-z
178. Dehesh T, Fadaghi S, Seyedi M, Abolhadi E, Ilaghi M, Shams P, et al. The relation between obesity and breast cancer risk in women by considering menstruation status and geographical variations: a systematic review and meta-analysis. BMC Womens Health. 2023;23:392. doi: 10.1186/s12905-023-02543-5
179. Arafat HM, Omar J, Muhamad R, Al-Astani TAD, Shafii N, Al Laham NA, et al. Breast cancer risk from modifiable and non-modifiable risk factors among Palestinian women: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2021;22(7):1987-95. doi: 10.31557/APJCP.2021.22.7.1987

180. Li H, Sun X, Miller E, Wang Q, Tao P, Liu L, et al. BMI, reproductive factors, and breast cancer molecular subtypes: a case-control study and meta-analysis. J Epidemiol. 2017;27(4):143-51. doi: 10.1016/j.je.2016.05.002
181. Cao Y, Ma J. Body mass index, prostate cancer-specific mortality, and biochemical recurrence: a systematic review and meta-analysis. Cancer Prev Res (Phila). 2011;4(4):486-501. doi: 10.1158/1940-6207.CAPR-10-0229
182. Tzenios N, Tazanios ME, Chahine M. The impact of body mass index on prostate cancer: an updated systematic review and meta-analysis. Medicine. 2022;101(45):e30191. doi: 10.1097/MD.0000000000030191
183. Discacciati A, Orsini N, Wolk A. Body mass index and incidence of localized and advanced prostate cancer--a dose-response meta-analysis of prospective studies. Ann Oncol. 2012;23(7):1665-71. doi: 10.1093/annonc/mdr603
184. Zhong S, Yan X, Wu Y, Zhang X, Chen L, Tang J, Zhao J. Body mass index and mortality in prostate cancer patients: a dose-response meta-analysis. Prostate Cancer Prostatic Dis. 2016;19(2):122-31. doi: 10.1038/pcan.2015.64
185. Golabek T, Bukowczan J, Chlosta P, Powroźnik J, Dobruch J, Borówka A. Obesity and prostate cancer incidence and mortality: a systematic review of prospective cohort studies. Urol Int. 2014;92(1):7-14. doi: 10.1159/000351325
186. González-Castro TB, Escobar-Chan YM, Fresan A, López-Narváez ML, Tovilla-Zárate CA, Juárez-Rojop IE, et al. Higher risk of depression in individuals with type 2 diabetes and obesity: results of a meta-analysis. J Health Psychol. 2021;26(9):1404-19. doi: 10.1177/1359105319876326
187. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. Obesity. 2013;21(3):E322-E7. doi: 10.1002/oby.20107
188. Koutoukidis DA, Knobf MT, Lanceley A. Obesity, diet, physical activity, and health-related quality of life in endometrial cancer survivors. Nutr Rev. 2015;73(6):399-408. doi: 10.1093/nutrit/nuu063
189. Jokela M, Laakasuo M. Obesity as a causal risk factor for depression: systematic review and meta-analysis of Mendelian randomization studies and implications for population mental health. J Psychiatr Res. 2023;163:86-92. doi: 10.1016/j.jpsychires.2023.05.034
190. Arango C, Dragioti E, Solmi M, Cortese S, Domschke K, Murray RM, et al. Risk and protective factors for mental disorders beyond genetics: an evidence-based atlas. World Psychiatry. 2021;20(3):417-36. doi: 10.1002/wps.20894
191. Lasikiewicz N, Myrissa K, Hoyland A, Lawton CL. Psychological benefits of weight loss following behavioural and/or dietary weight loss interventions. A systematic research review. Appetite. 2014;72:123-37. doi: 10.1016/j.appet.2013.09.017
192. Rittenberg V, Seshadri S, Sunkara SK, Sobaleva S, Oteng-Ntim E, El-Toukhy T. Effect of body mass index on IVF treatment outcome: an updated systematic review and meta-analysis. Reprod Biomed Online. 2011;23(4):421-39. doi: 10.1016/j.rbmo.2011.06.018
193. Sun Y-F, Zhang J, Xu Y-M, Cao Z-Y, Wang Y-Z, Hao G-M, Gao B-L. High BMI and insulin resistance are risk factors for spontaneous abortion in patients with polycystic ovary syndrome undergoing assisted reproductive treatment: a systematic review and meta-analysis. Front Endocrinol. 2020;11:592495. doi: 10.3389/fendo.2020.592495
194. Campbell JM, Lane M, Owens JA, Bakos HW. Paternal obesity negatively affects male fertility and assisted reproduction outcomes: a systematic review and meta-analysis. Reprod Biomed Online. 2015;31(5):593-604. doi: 10.1016/j.rbmo.2015.07.012
195. Campbell JM, McPherson NO. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: a systematic review and meta-analysis. Obes Res Clin Pract. 2019;13(6):511-21. doi: 10.1016/j.orcp.2019.11.003
196. Salas-Huetos A, Maghsoumi-Norouzabad L, James ER, Carrell DT, Aston KI, Jenkins TG, et al. Male adiposity, sperm parameters and reproductive hormones: an updated systematic review and collaborative meta-analysis. Obes Rev. 2021;22(1):e13082. doi: 10.1111/obr.13082
197. Sermondade N, Faure C, Fezeu L, Shayeb AG, Bonde JP, Jensen TK, et al. BMI in relation to sperm count: an updated systematic review and collaborative meta-analysis. Hum Reprod Update. 2013;19(3):221-31. doi: 10.1093/humupd/dms050
198. Wang S, Sun J, Wang J, Ping Z, Liu L. Does obesity based on body mass index affect semen quality?-A meta-analysis and systematic review from the general population rather than the infertile population. Andrologia. 2021;53(7):e14099. doi: 10.1111/and.14099
199. Moran LJ, Ko H, Misso M, Marsh K, Noakes M, Talbot M, et al. Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines. J Acad Nutr Diet. 2013;113(4):520-45. doi: 10.1016/j.jand.2012.11.018
200. Milone M, De Placido G, Musella M, Sosa Fernandez LM, Sosa Fernandez LV, Campana G, et al. Incidence of successful pregnancy after weight loss interventions in infertile women: a systematic review and meta-analysis of the literature. Obes Surg. 2016;26(2):443-51. doi: 10.1007/s11695-015-1998-7
201. Cronin O, Morris DR, Walker PJ, Golledge J. The association of obesity with cardiovascular events in patients with peripheral artery disease. Atherosclerosis. 2013;228(2):316-23. doi: 10.1016/j.atherosclerosis.2013.03.002
202. Baghdadi LR, Woodman RJ, Shanahan EM, Mangoni AA. The impact of traditional cardiovascular risk factors on cardiovascular outcomes in patients with rheumatoid arthritis: a systematic review and meta-analysis. PLoS ONE. 2015;10(2):e0117952. doi: 10.1371/journal.pone.0117952
203. Wang T, Zhang Q, Shi C, Gui S, Cao Z, Wang R, et al. Correlation between body mass index and mortality of patients with atrial fibrillation: a meta-analysis. Chin Nurs Res. 2020(20):3572-9. doi: 10.12102/j.issn.1009-6493.2020.20.002

204. Seo D-C, Choe S, Torabi MR. Is waist circumference ≥102/88cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. doi: 10.1016/j.ypmed.2017.01.012
205. Khadra D, Itani L, Tannir H, Kreidieh D, El Masri D, El Ghoch M. Association between sarcopenic obesity and higher risk of type 2 diabetes in adults: a systematic review and meta-analysis. World J Diabetes. 2019;10(5):311-23. doi: 10.4239/wjd.v10.i5.311
206. Lungu E, Maftoon S, Vendittoli PA, Desmeules F. A systematic review of preoperative determinants of patient-reported pain and physical function up to 2 years following primary unilateral total hip arthroplasty. Orthop Traumatol Surg Res. 2016;102(3):397-403. doi: 10.1016/j.otsr.2015.12.025
207. Romero JA, Jones R, Brown TS, Shahrestani SN, Huo MH. Morbid obesity in total hip arthroplasty: what does it mean? Semin Arthroplasty. 2017;28(4):254-8. doi: 10.1053/j.sart.2018.02.013
208. van Tilburg J, Rathsach Andersen M. Mid- to long-term complications and outcome for morbidly obese patients after total knee arthroplasty: a systematic review and meta-analysis. EFORT Open Rev. 2022;7(5):295-304. doi: 10.1530/EOR-21-0090
209. Si H-b, Zeng Y, Shen B, Yang J, Zhou Z-k, Kang P-d, Pei F-x. The influence of body mass index on the outcomes of primary total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23(6):1824-32. doi: 10.1007/s00167-014-3301-1
210. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019;20(1):493. doi: 10.1186/s12891-019-2895-3
211. Australian Bureau of Statistics. Waist circumference and BMI [Internet] Canberra: ABS; 2022 [cited 2024 August 13]. Available from: https://www.abs.gov.au/statistics/health/health-conditions-and-risks/waist-circumference-and-bmi/latest-release.
212. Menigoz K, Nathan A, Turrell G. Ethnic differences in overweight and obesity and the influence of acculturation on immigrant bodyweight: evidence from a national sample of Australian adults. BMC Public Health. 2016;16(1):932. doi: 10.1186/s12889-016-3608-6
213. Khatri RB, Assefa Y. Access to health services among culturally and linguistically diverse populations in the Australian universal health care system: issues and challenges. BMC Public Health. 2022;22(1):880. doi: 10.1186/s12889-022-13256-z