NIHR | Policy Research Unit in Obesity

OPRU Briefing Paper - Assessing the evidence for health benefits of low levels of weight loss: a systematic review

Jessica Packer, Disha Dhar, Semina Michalopoulou, Joana Cruz, Simon Russell

Key messages

In the UK, weight loss of less than 5% is the most common outcome from lifestyle weight loss interventions. It is useful for policy makers to understand what, if any, health benefits there are of achieving low weight loss (less than 5% of body weight).

To provide evidence to answer this question, we systematically searched the international academic literature to explore the health benefits of losing a low amount of weight (0-5% body weight loss).

We have described where low weight loss led to health benefits by health outcome. Typically, these include cardiovascular (e.g., triglycerides and total cholesterol), metabolic (e.g., leptin and adiponectin), anthropometric (e.g., waist circumference and visceral fat), inflammatory biomarkers (e.g., interleukins). We have also described findings by intervention type i.e., lifestyle (diet and/or physical activity), pharmacological or interventions that combine both.

We included 70 intervention studies (from 68 articles) that reported low weight loss or stratified health outcomes by weight loss, including a group (or groups) of less than 5%.

- Overall, 60% of studies found health improvements, 37% found no change or mixed results, and 3% found worsening of health outcomes.
- Studies that found health improvements included 87% of total participants, but not all studies reported the number of participants by weight loss group (e.g., <5%) and we cannot say what number/proportion of participants had health improvements.
- We found evidence that low weight loss led to improvements in a wide range of health outcomes, including cardiovascular and metabolic, anthropometric, quality of life, inflammatory biomarkers, renal and hepatic, psychosocial and behavioural, pulmonary, and ovulatory function.
- Weight loss achieved by both lifestyle and drug interventions led to improvements in all health outcomes, except for total mortality, pulmonary function and muscle strength (all lifestyle interventions), and psychosocial and behavioural measures (lifestyle and drug interventions).
- Three studies were from the UK and more than 90% of the studies were conducted in high income countries.
- Due to the heterogeneity of the results meta-analysis was not possible.
- Generally, we found studies had moderate bias. Typical issues were around randomisation methodology or reporting.

Executive summary

Background

In the UK, the prevalence of excess weight (including overweight and obesity) is high and increasing. The burden of excess weight is costly, with estimates that by 2050 it will cost the National Health Service £9.7 billion and wider society £49.9 billion.

It is evident in the literature that weight loss has health benefits, but it is unclear at what threshold. Modest weight loss, defined as greater than 5%, is often viewed by medical professionals as the threshold to reach in order to see clinically meaningful health benefits. There is little evidence around the benefits of less than 5% weight loss, given that guidelines often focus on the 5% threshold. The evidence that does exist focuses primarily on cardiovascular and metabolic outcomes and in people with pre-existing health conditions.

Weight loss of less than 5% body weight is the most common outcome from lifestyle interventions in the UK. It is therefore important for policy makers to understand the health benefits of achieving low weight loss (less than 5% of body weight).

We conducted a systematic review of published literature that examined a wide range of possible health benefits, to provide evidence to meet this evidence gap and to inform the thinking of policy makers.

Aim

We aimed to review and synthesise the international evidence to better understand the potential health benefits of low weight loss (0-5% body weight) including indicators of cardiovascular, metabolic, physical and psychosocial health.

Executive summary

What we did

We searched six academic databases and included studies in any language, from any country, with no time constraints. We included any intervention studies that assessed the impact of low weight loss (defined as less than 5% body weight) on any measured health outcomes.

We excluded non-peer-reviewed grey literature, modelling studies, systematic reviews, commentaries, editorials, or conference abstracts. We completed bias and quality assessments for all included studies.

What we found

We included a total of 70 intervention studies (68 articles; 42 RCTs, and 28 non-RCTs).

- Most evidence came from the USA (n = 34), Canada (n = 3), UK (n = 3), and Australia (n = 2).
- Interventions included, lifestyle interventions (n = 47), pharmacological interventions (n = 2) or a combination of both (n = 21).
- The main weight loss stratification was less than 5% (n = 42), followed by less than 3% (n = 7), and greater than 2 to less than 5% (n = 7).
- We broadly categorised health outcomes as: cardiovascular markers (n = 32), metabolic markers (n = 42), anthropometric measures (n = 19), quality of life outcomes (n = 10), inflammatory biomarkers (n = 10), renal and hepatic markers (n = 9), psychosocial and behavioural measures (n = 8), pulmonary function (n = 3), total mortality (n = 2), ovulatory function (n = 1), and muscle strength (n = 1).
- Overall, 60% of studies (87% of participants) found health improvements, 37% found no change or mixed results, and 3% found worsening of health outcomes.

Background

In 2021-22, the prevalence of excess weight (overweight and obesity) in adults in England was estimated to be 63.8% (see Figure 1).[1] This was a slight increase from 2020-21 (63.3%), and a marked increase from 1993 levels (52.9%; see Figure 2).[1] Obesity is estimated to cause more than 30,000 deaths per year and deprive individuals of an average of 9 years of life.[2] Excess weight-related ill health in the UK is estimated to have cost the National Health Service (NHS) £6.1 billion in 2014-15; a figure projected to reach £9.7 billion by 2050.[2] There are wider costs to society, including the loss of quality adjusted life years and productivity, which were reported to cost £27 billion in 2017 and projected to reach £49.9 billion by 2050.[2]

Figure 1: Overweight and obesity prevalence in England (2021)[1]

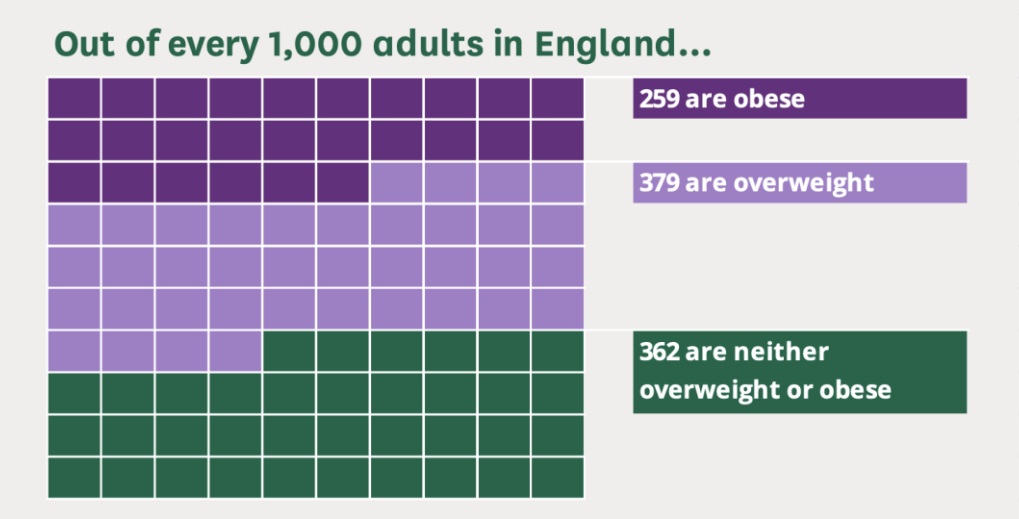
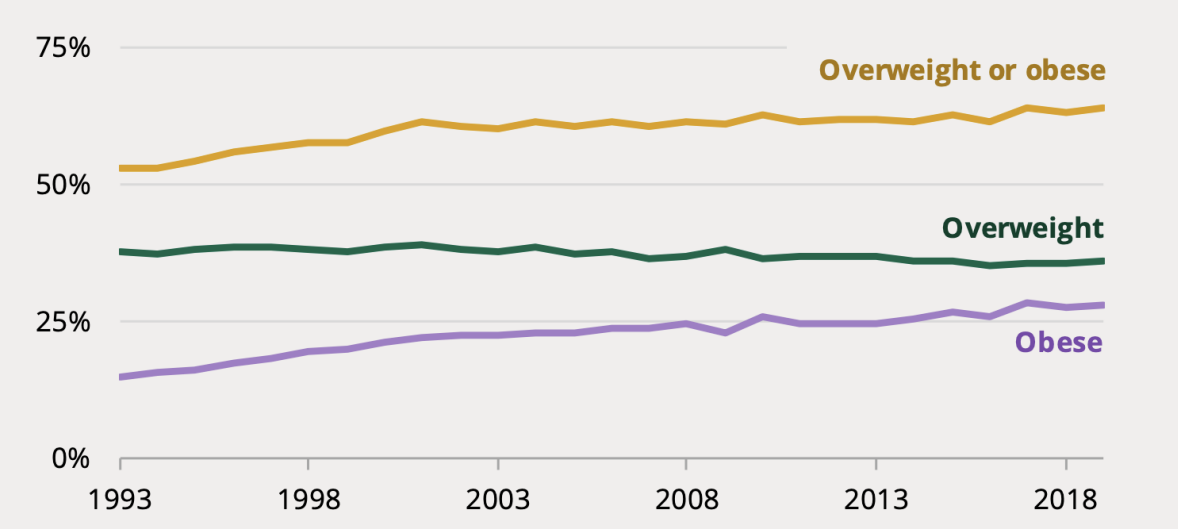


Figure 2: Trend in overweight and obesity prevalence from 1993 to 2018[1]

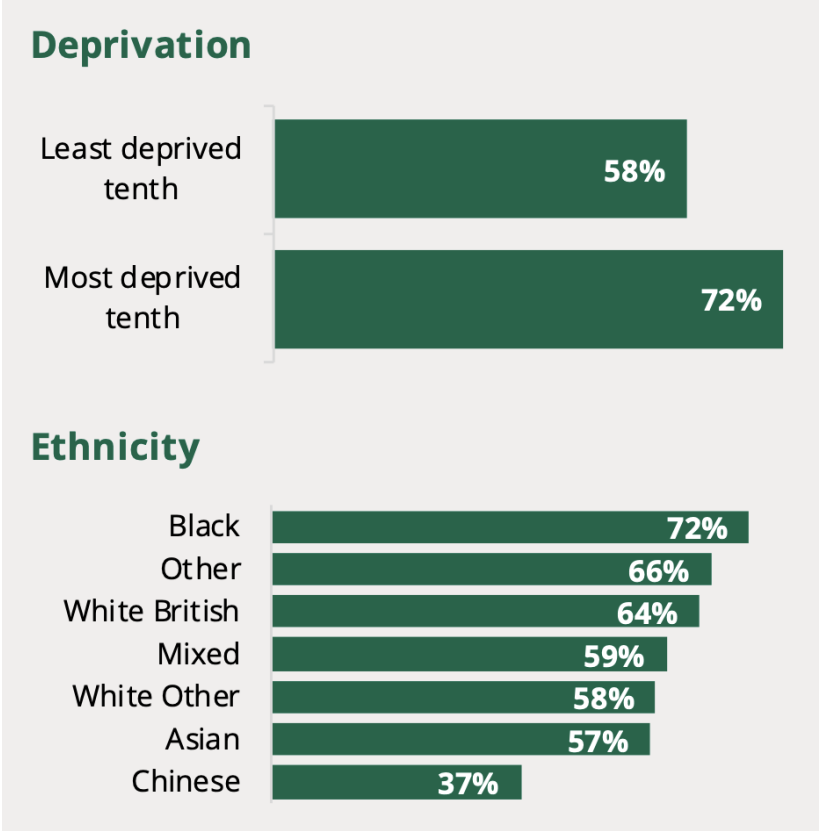


1. Baker (2023) Obesity statistics – Research Briefing. House of Commons Library. https://researchbriefings.files.parliament.uk/documents/SN03336/SN03336.pdf
2. Public Health England (2017) Guidance - Health matters: obesity and the food environment. https://www.gov.uk/government/publications/health-matters-obesity-and-the-food-environment/health-matters-obesity-and-the-food-environment--2

Background

- People living with obesity are at an increased risk of developing a range of diseases, including cardiovascular diseases (such as stroke or heart attacks), cancer (at least 12 kinds), liver disease, type-2 diabetes, respiratory disease (such as asthma) and mental health difficulties, including anxiety and depression.[3,4]
- Inequalities in overweight and obesity are stark; prevalence of excess weight in the most deprived areas in England are considerably higher, compared to in the least deprived areas (72% vs 58%). There are also inequalities in the burden of disease; adult hospital admissions directly attributable to obesity are more than three times higher in the most deprived compared to least deprived areas.[1,5] There are differences by ethnicity, with the highest prevalence found among black adults (72%) compared to white British (64%), or mixed (59%; Figure 3).[1] The burden and risk threshold of disease with obesity is also different by ethnic group regardless of SES, with analyses from the UK and US showing disproportionate burden and disease risk for non-white populations.[6,7]

Figure 3: Prevalence of excess weight by deprivation and ethnicity in England (2020-21)

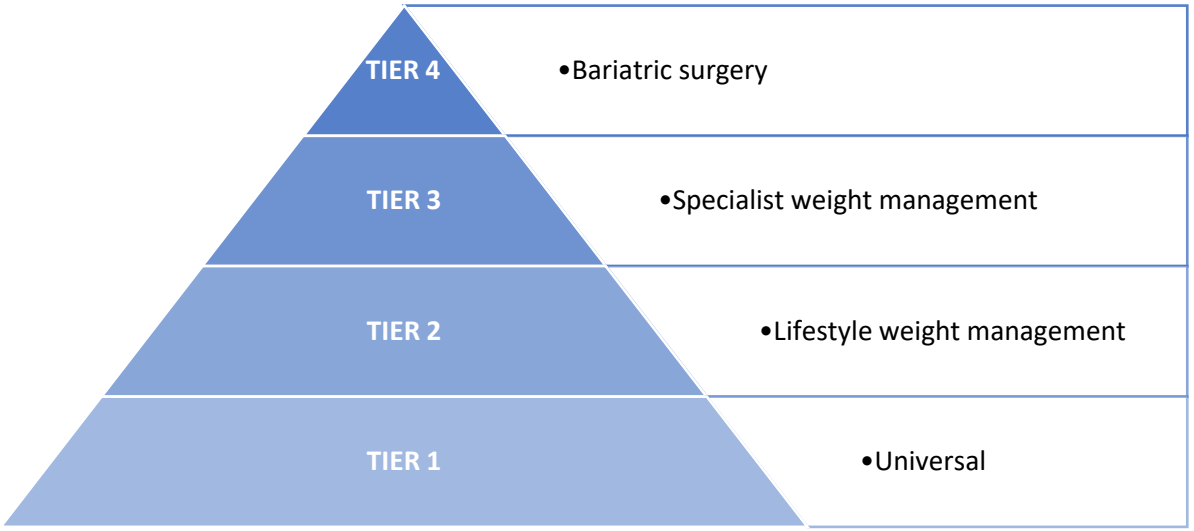


3. Guh et al. (2009) The incidence of co-morbidities related to obesity and overweight: A systematic review and meta-analysis. https://doi.org/10.1186/1471-2458-9-88
4. Luppino et al. (2010) Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. https://doi.org/10.1001/archgenpsychiatry.2010.2
5. NHS Digital (2021) Statistics on Obesity, Physical Activity and Diet, England 2021. https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/england-2020/part-3-adult-obesity-copy
6. Caleyachetty et al. (2021) Ethnicity-specific BMI cutoffs for obesity based on type 2 diabetes risk in England: a population-based cohort study https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00088-7/
7. Okobi et al. (2023) Trends in Obesity-Related Mortality and Racial Disparities https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10403782/

Background

One method of reducing excess weight is through the delivery of evidence-based weight management (WM) services, as set out in the National Institute for Health and Care Excellence (NICE) guidance (updates to this guidance are in development).[6,7] In England, there is a tiered approach to WM services, with treatment and intensity dependent on the level of excess weight and presence of comorbidities (see Figure 4). Typically, tier 1 refers to universal services, tier 2 refers to lifestyle WM services, tier 3 refers to specialist WM services (including drug interventions), and tier 4 refers to bariatric surgery.[8] The average length of tier 2 WM services is 12 weeks; with research showing a weight loss of ~2% is a common outcome for a 12-week intervention.[9,10]

Figure 4: Tiered weight management services in England



8. NICE (2016) Obesity in adults: prevention and lifestyle weight management programmes https://www.nice.org.uk/guidance/qs111
9. NICE (2024) Overweight and obesity management https://www.nice.org.uk/guidance/indevelopment/gid-ng10182
10. Public Health England (2015) National mapping of weight management services. https://assets.publishing.service.gov.uk/media/5a7f74d2e5274a2e8ab4c4b1/Final_Weight_Management_Mapping_Report.pdf
11. Public Health England (2021) Better Health campaign Phase 1: evaluation of the NHS weight loss plan app https://assets.publishing.service.gov.uk/media/61265801e90e070541075822/Evaluation_of_the_NHS_App_PHE_Report_25Aug2020.pdf
12. Tate et al. (2012). Replacing caloric beverages with water or diet beverage for weight loss in adults: Main results of the Choose Healthy Options Consciously Everyday (CHOICE) randomized clinical trial.

Background

- Various approaches can be used to measure weight loss, including change in BMI or body fat, or percentage change in body weight or fat mass. This report considers percentage change in body weight as it is a commonly reported, proportionate measure that allows for stratification and comparison between participants and interventions; it also allows for exploration of clinically and policy relevant thresholds.
- Weight loss of greater than 5% of baseline weight is generally accepted as providing clinically meaningful benefits and is often the standard goal for weight loss interventions.[13-15] While some adults achieve moderate/high weight loss (5 - <10%/10% or more), many will achieve less than 5% body weight (defined in this report as low).
- Some studies have examined the effect of weight loss of less than 5% body weight, but gaps in evidence remain. Two reviews focused on cardiovascular health outcomes, finding that weight loss between 3-5%; or 0-<2.5% and 2.5-<5% led to improvements in cardiovascular risk factors.[16, 17] One review focused on adults with pre-existing cardiovascular risk factors; while the other used mean weight loss across an intervention group, thereby not assessing the impact of less than 5% weight loss exclusively. Another review examined broader health outcomes, including quality of life, fertility, mental health and physical health, but they provided no search strategy or protocol.[18] They found weight loss of 2.5% or more led to improvements beyond cardiovascular/metabolic, such as improvements in fertility and ovulatory cycles.
- To inform policy thinking on WM services, we conducted a robust, comprehensive and up-to-date review assessing the evidence on the health benefits (including cardiovascular and wider health outcomes) of low weight loss (specifically less than 5% body weight).

Primary aims

- To systematically review the evidence assessing the health benefits of losing a low amount of weight (0-5% weight loss) on health benefits including cardiometabolic, physical and psychosocial.

Secondary aims

To synthesize results, if data allow, by:

- Starting body mass index
- Different levels of weight loss
- Type of intervention (lifestyle/ pharmacological)

13. Varkevisser et al. (2019) Determinants of weight loss maintenance: a systematic review https://doi.org/10.1111/obr.12772
14. Donnelly et al. (2009) American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. https://doi.org/10.1249/MSS.0b013e3181949333
15. Williamson et al. (2015) Is 5% weight loss a satisfactory criterion to define clinically significant weight loss? https://doi.org/10.1002/oby.21358
16. Jensen et al. (2014) Expert panel report: Guidelines (2013) for the management of overweight and obesity in adults https://doi.org/10.1002/oby.20660
17. Zomer et al. (2016) Interventions that cause weight loss and the impact on cardiovascular risk factors: a systematic review and meta-analysis. Obesity Reviews. https://doi.org/10.1111/obr.12433
18. Ryan & Yockey (2017) Weight Loss and Improvement in Comorbidity: Differences at 5%, 10%, 15%, and Over. Current obesity reports. https://doi.org/10.1007/s13679-017-0262-y

Methods

- In March 2023 we searched six academic databases for evidence relating to the impact of less than 5% weight loss. We also conducted 'citation searches' to capture other relevant studies.
- We included studies from all countries and in any language; that were peer-reviewed academic literature.
- We were only interested in non-surgical weight loss intervention studies; both pharmacological or lifestyle (diet or exercise), or a combination of both.
- We were particularly interested in studies where participants had no pre-existing conditions. We did include studies where participants had pre-existing conditions, but only if the focus of the intervention was weight loss.
- We included anthropometric health outcomes, such as waist and hip circumference, as despite being related to BMI, they are also standalone indicators of health, relating closely to visceral/intra-abdominal fat.[19]
- We excluded studies with adults classified as underweight, as they are outside the scope of relevant WM guidelines; bariatric surgery, as it is an invasive intervention with initial weight loss likely to be greater than 5% body weight; any study that did not provide outcomes stratified by participants who achieved less than 5% body weight.
- EPPI-Reviewer Version 6 was used for the screening and review management.[20] We prospectively registered the review with PROSPERO (CRD42023406342).[21]
- Risk of bias was assessed for all studies using a Critical Appraisal Skills Programme (CASP) checklists.[22]

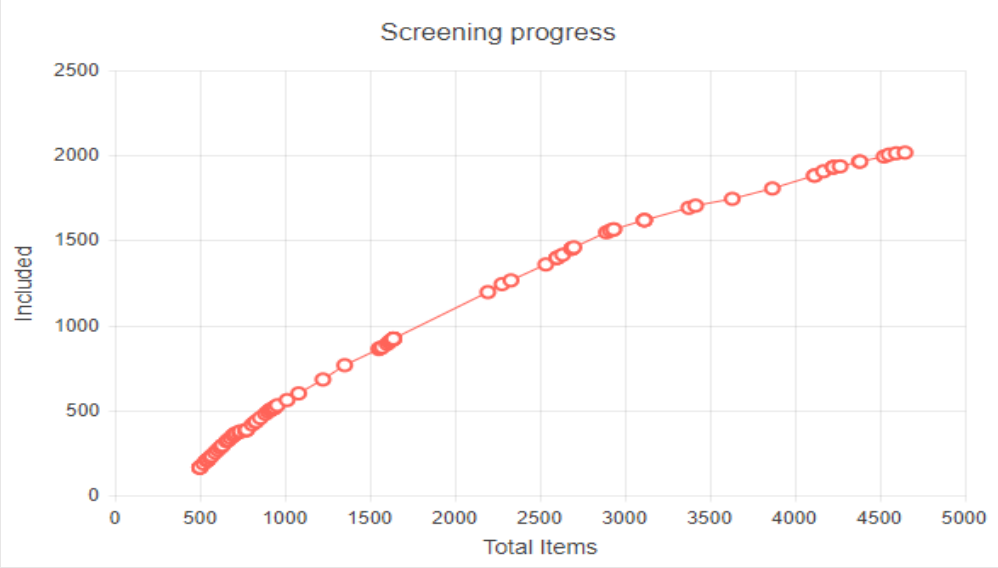
Inclusion criteria	Exclusion criteria
Adults (18 years+)	Participants aged 17 years and under; Underweight (Body mass index <18.5)
Non-surgical weight loss intervention studies (lifestyle or pharmacological)	Bariatric surgery
Weight loss of less than 5% bodyweight due to a weight loss intervention	Mean weight loss reported only i.e., overall intervention effect; stratified weight loss not between 0-5%, or percentage not reported
All countries, languages, publication dates, peer-reviewed	Non-peer reviewed studies

19. Ross et al. (2020) Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity https://doi.org/10.1038/s41574-019-0310-7 d
20. Thomas, J., et al., *EPPI-Reviewer: advanced software for systematic reviews, maps and evidence synthesis*. 2022: EPPI Centre, UCL Social Research Institute, University College London
21. https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023406342
22. Critical Appraisal Skills Programme (2023). CASP Randomised Controlled Trial Checklist. [online] Available at: https://casp-uk.net/casp-tools-checklists/.

Methods

- There were a total of 8,127 articles from academic databases included for screening (see Appendices 1 and 2 for search terms and flow chart). Three reviewers (JP, SM, JC) independently double-screened the articles on title and abstract, and full-text.
- Using the EPPI-Reviewer software we used an 'active learning approach' where, prioritisation of records was periodically refreshed during screening, in order that the most relevant articles were screened first.
- A graphical output was used to indicate when to stop screening, i.e., when the number of relevant studies had plateaued (see Figure 5). A model was then built using the machine learning algorithm and applied to classify unscreened items with a score that indicates likely relevance; the classifier model reduces the likelihood that relevant studies would be missed.
- In total, 4,912 articles were manually screened. During title and abstract screening, 3,943 articles were excluded manually, and 3,215 articles were excluded using the classifier score. There were 969 articles included for full text screening, of which 902 articles were manually excluded or we were unable to retrieve the full-text. One additional article was included from citation searching, giving a total of 68 included articles (70 studies).

Figure 5: Screening progress graph



Methods

- We extracted the following data: study characteristics (primary author, publication year, country, study design, sample size, intervention characteristics (e.g., intervention duration), weight loss stratification categories, and the key findings.
- Risk of bias was assessed by three reviewers (SM, DD, JP) using the CASP checklist.[22] All discrepancies were jointly reconciled.
- Data were synthesised narratively with descriptive characteristics. Meta-analysis was not possible due to the stratification of the outcomes by weight-loss groups and inconsistent reporting of values (i.e., overall baseline or by intervention group, but follow-up outcomes only reported by weight loss groups; missing sample sizes; missing precision estimates).
- The number of participants that lost less than 5% body weight was identified and extracted from included studies, where reported.

- We were interested in these subgroups, as set out a priori:
  - Type of intervention (lifestyle/ pharmacological)
  - Health outcome
  - Starting BMI

Weight loss definitions	
Low	0 - <5%
Moderate	5% - <10%
High	10% or more

Description of studies

Description of studies

70 studies were included in the final analysis, assessing a total of 137 health outcomes (see Table 2 for an overall summary, Appendix 3 for the full reference list and the supplementary file for further details).

Studies were conducted in the USA (n = 34), Europe (n = 15: UK = 3, Finland = 2, Italy = 2, Spain = 2, Belgium = 1, Greece = 1, Germany = 1, Poland = 1, Romania = 1, and Serbia = 1), Canada (n = 3), Japan (n = 3), Australia (n = 2), South Korea (n = 2), Brazil (n = 1), China (n = 1), Malaysia (n = 1), Taiwan (n = 2) or across multiple countries (n = 6).

More than 90% of the included studies were conducted in high-income countries.

The majority of studies were randomised controlled trials (n = 42), with the remaining study designs (n = 28) including intervention studies, clinical trials, cohort studies, prospective studies and secondary analyses of trials or interventions.

Interventions identified in the following studies were sub-divided into lifestyle (n = 47), pharmacological (n = 2), or a combination of both lifestyle and pharmacological (n = 21). The most common drug utilised for pharmacological interventions was Orlistat (n = 5), Sibutramine (n = 4) and Metformin (n = 2).

Benefits from less than 5% weight loss were seen from 6 weeks after baseline, the earliest follow-up timepoint from included studies (Sharma et al.),[23] and as late as 7.4 years (Rintamaki et al.),[24] see the descriptive table in the supplementary file for further details.

23. Sharma et al. (2009) Blood pressure changes associated with sibutramine and weight management - an analysis from the 6-week lead-in period of the sibutramine cardiovascular outcomes trial (SCOUT).
24. Rintamaki et al. (2021) Long-term outcomes of lifestyle intervention to prevent type 2 diabetes in people at high risk in primary health care.

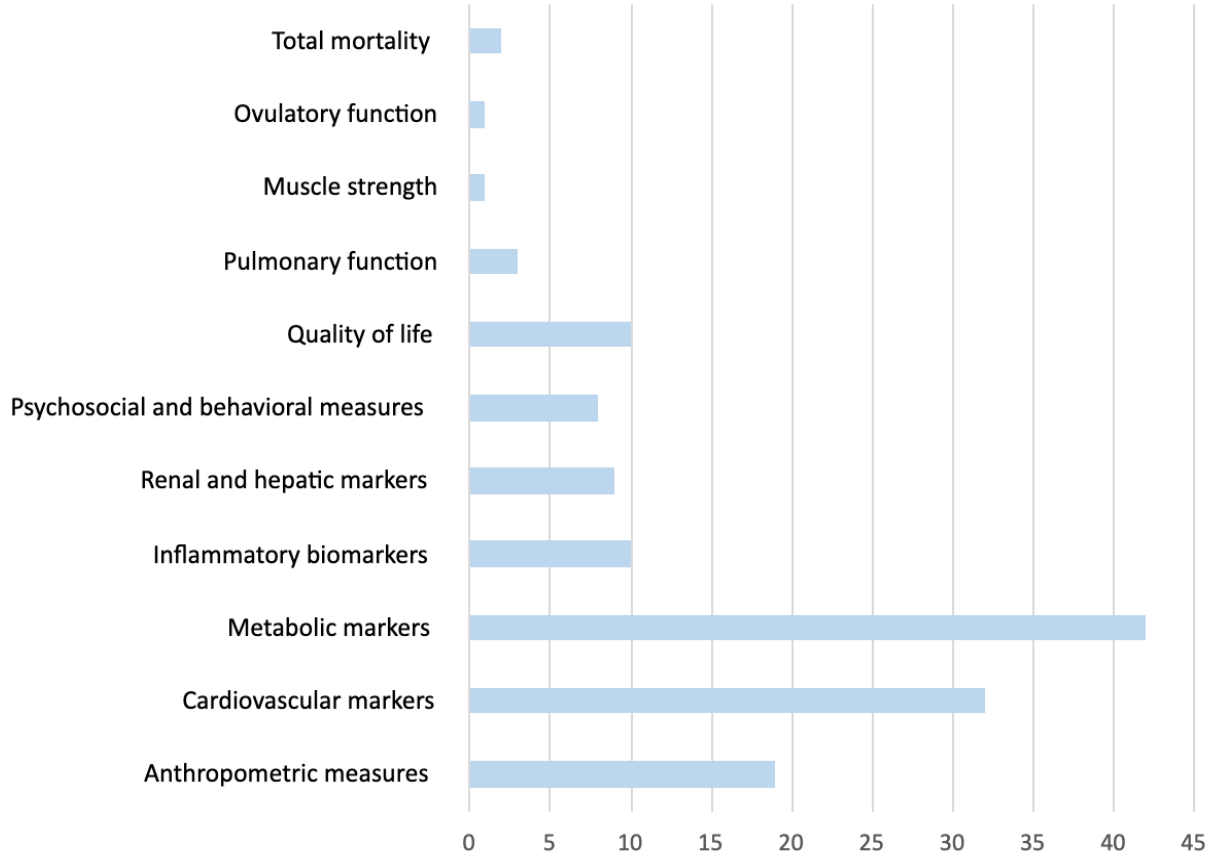
Description of studies

Description of studies continued.

Health outcomes from included studies were: metabolic markers (n = 42; including fasting glucose/insulin and HbA1c), cardiovascular markers (n = 32; including systolic and diastolic blood pressure, total cholesterol, triglycerides), anthropometric measures (n = 19; including waist circumference, body fat percentage and visceral fat mass), quality of life outcomes (n = 10; including Apnea–Hypopnea Index and The Pittsburgh Sleep Quality Index), inflammatory biomarkers (n = 10; including high-sensitivity C-reactive protein and different interleukins), renal and hepatic markers (n = 9; including fatty liver index and uric acid), psychosocial and behavioural measures (n = 8; including Brief Symptom Rating scale and 6-minute walk test), pulmonary function (n = 3), total mortality (n = 2), ovulatory function (n = 1), and muscle strength (n = 1).

See Panel 1 for outcomes in full and the supplementary file for an in-depth description of the health outcomes from included studies.

Figure 6: Health outcomes of the included studies



Panel 1: Specific outcomes from included studies

Cardiometabolic	Diastolic blood pressure, systolic blood pressure, blood pressure, mean arterial pressure, triglycerides, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, mean non- high-density lipoprotein cholesterol, total high-density lipoprotein cholesterol ratio, small low-density lipoprotein cholesterol, large high-density lipoprotein cholesterol, low-density lipoprotein cholesterol particles, TC/HDL-C ratio, protein intake, P wave dispersion, and CVD incidence
Metabolic	Adiponectin, leptin, fasting plasma glucose, fasting insulin, fasting serum insulin, fasting glucose, HbA1c, HOMA-IR, HOMA2-β, Matsuda index, 30-min insulin, AUC glucose/insulin, sum of insulin concentrations, carbohydrate-to-insulin ratio, 2h-PG, FSI, insulin sensitivity, glucose effectiveness, acute insulin response, FS leptin, adipocyte cell size, C-reactive protein, IGF-1, diabetes risk, diabetes incidence, fasting total serum ghrelin, irisin, fibrosis, controlled attenuation parameter, microbiome, DNA repair capacity, radiation sensitivity, metabolic syndrome severity Z-score and metabolic syndrome components, metabolic syndrome incidence and escape rate, vaspin, C-peptide, fibrinogen, resting energy expenditure, estrone, estradiol, total testosterone, sex hormone–binding globulin, free estradiol, free testosterone, Urinary 8-isoprostanes, sNOX2-dp, vitamin E, vitamin E/cholesterol ratio, and bone marrow fat content
Anthropometric	Waist circumference, hip circumference, abdominal circumference, % body fat, fat mass, fat free mass, trunk fat mass, visceral fat area, visceral fat mass, visceral adipose tissue, body fat composition, subcutaneous fast mass, lean body mass, android fat, and gynoid fat
Quality of life	Sleep duration and quality (PSQI), sleep mood (PHQ-8), sleep disturbance, Apnoea-Hypopnea Index, NREM-AHI, REM-AHI, HI, AI ODI and SaO2, AQLQ domains, asthma control score, IWQOL-Lite scores, EQ-5D scores, SF-36 scores, OWLQOL score, WSRM bother scores, physical functioning, pain, social functioning, role functioning, mental health, health perceptions, self-efficacy, perceived risk for heart disease and diabetes, impact of weight on QOL-Lite, urinary incontinence per week (total, stress and urge), 24-hour involuntary urine loss, and satisfaction with changes with incontinence
Inflammatory biomarkers	TNF-α, hs-CRP, IL1β, IL6 IL8, IL10, and Inflammatory Biomarker Score, oxidized LDL, fluorescent oxidation products, F2-isoprostanes, resistin, airway inflammation, interleukins, vascular endothelial growth factor, vitamin D, SAA, leukocytes, and neutrophils
Renal and hepatic	AGT, MDA, MCP-1, podocalyxin, 24-hr Una/Cr, eGFR, albuminuria, albumin, bilirubin, GGT, FLI, NAFLD-fibrosis score, uric acid, ALT, AST, γGTP, GGT, fatty liver index, AST/ALT, FI and APRI
Psychosocial and behavioural	Physical activity- and eating-related self-regulation, self-efficacy, mood, emotional eating, physical function, sexual function, endocrine symptoms, pain interference, fatigue, depression, anxiety, sleep disturbance, total body esteem, appearance, attribution, self-esteem, stress, dietary restraint, disinhibition, hunger, physical activity MET hrs/week, exercise fatigue level, 6-min walk test, exercise frequency, fat in diet, PHQ-9 depression score, Brief Symptom Rating Scale, Bulimic Investigatory Test, Edinburgh, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health, PCS scores, and MCS scores
Pulmonary function	FRC, ERV, RV, IC, TLC, FEV1, FVC, FEV1/FVC ratio, ACQ, AQLQ, St. George's Respiratory Questionnaire
Muscle strength	Quadriceps muscle strength and endurance

Description of studies

Description of studies continued..

The participants' average baseline BMI was categorised using NICE guidelines,[25] as overweight (n = 4), obesity class-1 (n = 35), obesity class-2 (n = 23), obesity class-3 (n = 1), mixed categories (n = 2), or not reported (n = 5). We were unable to synthesise results by baseline weight status as mean BMI was reported for groups overall and without knowing the distribution, reliable comparisons between studies could not be drawn.

For the stratification of health outcomes by low weight loss groups, most of the studies examined the results by weight loss less than 5% (n = 42), or less than or equal to 5% (n = 5); some studies used lower cut-offs of less than 2%/3% (n = 1/n = 7); while other studies examined results by weight loss between 2 and less than 5% (n = 7); some studies included multiple categories that were less than 5%, such as a 0-3% group, and a 3-5% group (n = 7), and one study examined outcomes per 1% body weight loss (n = 1).

Studies with multiple low weight loss categories

We included 7 studies, that examined multiple low weight loss categories. For two of the studies, the higher weight loss group (2.5-5%; >2% to ≤4.5%) showed an improvement in the measured health outcomes that was not observed in the lower weight loss group (0-2.5%; ≤2%). For the other five studies the results were the same across the categories.

Bias assessment

The studies were assessed for bias and quality (see Appendix 4). Overall, there was moderate bias, with domains that showed typical issues were around randomisation methodology or reporting.

25. National Institute for Heath and Care Excellence (2023). Obesity. https://cks.nice.org.uk/topics/obesity/diagnosis/identification-classification/

Intervention characteristics

Table 2. Descriptive summary of intervention characteristics

Intervention type (n = 70)	N (%)
Lifestyle	47 (67%)
Pharmacological	2 (3%)
Combination of lifestyle and drug interventions	21 (30%)
Health outcomes* (n = 137)	**N (%)**
Metabolic markers	42 (31%)
Cardiovascular markers	32 (23%)
Anthropometric measures	19 (14%)
Quality of life outcomes	10 (7%)
Inflammatory biomarkers	10 (7%)
Renal and hepatic markers	9 (7%)
Psychosocial and behavioural measures	8 (6%)
Pulmonary function	3 (2%)
Total mortality	2 (1%)
Ovulatory function	1 (1%)
Muscle strength	1 (1%)

*Greater than the number of studies, as some included more than one health outcome or **comorbidity

Participant inclusion criteria BMI (n = 70)	N (%)
Overweight (BMI 25-29.9 kg/m$_2$) and higher	42 (60%)
Obesity class 1 (BMI 30-34.9 kg/m$_2$) and higher	9 (13%)
Obesity class 2 (BMI 35-39.9 kg/m$_2$) and higher	1 (1%)
Obesity class 3 (BMI 40 kg/m$_2$ or more)	-
Not reported	18 (26%)
Participant comorbidities (n = 75)**	**N (%)**
None	34 (45%)
Metabolic syndrome$^+$	18 (24%)
Diabetes	8 (11%)
Hepatic disorders	6 (8%)
Asthma	2 (3%)
Obstructive sleep apnea	2 (3%)
Cardiovascular disease	2 (3%)
Polycystic ovary syndrome	1 (1%)
Urinary incontinence	1 (1%)
Idiopathic pulmonary fibrosis	1 (1%)

$^+$Metabolic syndrome - a cluster of conditions that occur together, increasing your risk of heart disease, stroke and type 2 diabetes, e.g. hypertension, dyslipidemia, and hypercholesterolemia

Overview of Results

We examined the proportion of weight loss interventions that stratified the health outcome results by participants who lost between 0-5% of their bodyweight, since the start of the intervention, in terms of the proportion that led to an improvement in the health outcome.

Table 3. Summary of study results

Study findings (n = 70)	*N (studies)*	% studies	N/% of participants that lost less than 5% body weight	Studies that found statistical significance (n = 36)
Improvements in health outcomes	42	60%	15,839* (86.6%)	21
Worsening in health outcomes	2	3%	20* (0.1%)	2
Studies that observed no-significant changes	2	3%	103 (0.6%)	-
Studies that observed mixed changes	24	34%	2,325* (12.7%)	13

*Not all included studies provided a sample size for the <5% body weight loss category.

Overall

- **60% of studies found that low weight loss following an interventions led to improvements in health outcome.**

Participants from these studies represented 86.6% (15,839) of participants where sample sizes were reported, which represents strong evidence; however, most included studies had moderate bias, often for issues around randomisation or reporting.

- **34% of studies found mixed results – some health outcomes improved and some worsened**
- **3% of studies found no change**
- **3% of studies found worsening health outcomes**

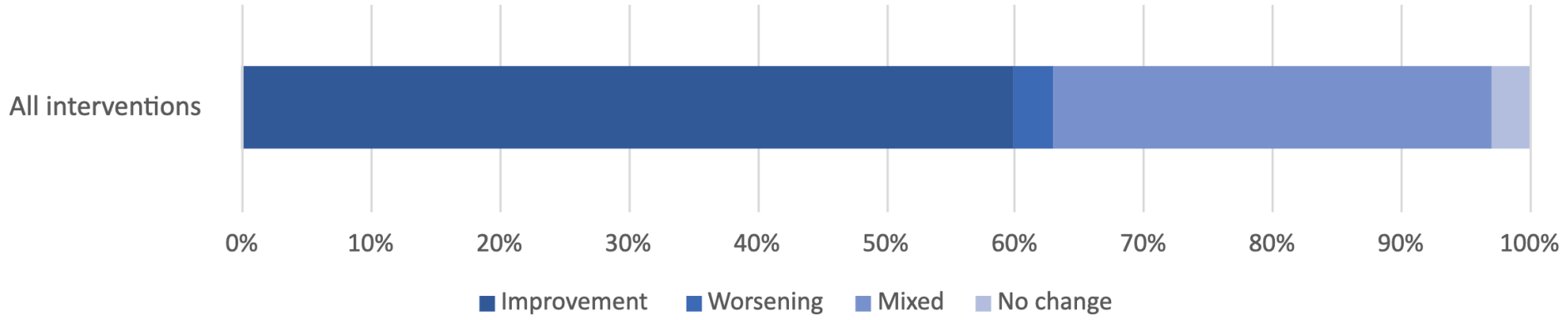
Results by intervention type

Table 4. The proportion of studies and intervention types that led to a change in health outcomes

Studies by intervention type	Improvement	Worsening	Mixed results	No change
Lifestyle (*n* = 47)	29 (62%)	2 (4%)	15 (32%)	1 (2%)
Pharmacological (*n* = 2)	2 (100%)	-	-	-
Both lifestyle and pharmacological* (*n* = 21)	11 (52%)	-	9 (43%)	1 (5%)
All studies / intervention types (n = 70)	42 (60%)	2 (3%)	24 (34%)	2 (3%)

*It was not possible to distinguish the impact of individual interventions

Figure 7. The proportion of studies reporting interventions that led to a change in health outcomes



Findings by health outcomes

Table 5. Proportion of interventions that led to improvements in health outcome by condition (n = 137)

Health outcome	Improvement (%)	Worsening (%)	Mixed results (%)	No change (%)	Total studies	Number of participants (loss <5% body weight)
Metabolic	22 (52%)	3 (7%)	13 (31%)	4 (10%)	42	9,389*
Cardiovascular	18 (56%)	1 (3%)	8 (25%)	5 (16%)	32	13,139*
Anthropometric	17 (89%)	-	-	2 (11%)	19	5,004
Quality of life	6 (60%)	2 (20%)	2 (20%)	-	10	1,222
Inflammatory biomarkers	6 (60%)	-	3 (30%)	1 (10%)	10	795*
Renal and hepatic	9 (100%)	-	-	-	9	1,783*
Psychosocial and behavioural	4 (50%)	-	1 (12%)	3 (38%)	8	702
Pulmonary function	1 (33%)	1 (33%)	-	1 (33%)	3	774
Total mortality	-	1 (50%)	-	1 (50%)	2	642
Ovulatory function	1 (100%)	-	-	-	1	11
Muscle strength	-	-	-	1 (100%)	1	23

*Not all included studies provided a sample size for the <5% body weight loss category.

Case studies

Case study – UK

Three of the included studies were conducted exclusively in the UK[26-28] (see the descriptive table in the supplementary file for more detail). The most recent study was conducted by Strelitz et al (2019).

- A cohort analysis among 725 adults with screen-detected diabetes enrolled in a cluster randomised trial. The study investigated the effect of lifestyle interventions (consultations, educational materials and GP-based academic sessions on risk factors) on incidence of CVD events and all-cause mortality.
- Key findings: Within the ≥2 to <5% weight loss group, at both 1 and 5 years there were improvements in cardiovascular (systolic blood pressure, diastolic blood pressure, triglycerides, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and CVD incidence) and metabolic markers (HbA1C).

Case studies of multiple weight loss categories

Seven of the included studies had multiple low weight loss categories, of which two found different results between the groups.

- Muls et al (2001)[29] was a 24-week RCT that examined the low-density lipoprotein cholesterol (LDL-C) by weight loss of 0-2.5% and 2.5-5%. They found that LDL-C only consistently decreased in the 2.5-5% weight loss group.
- Spurny et al (2020)[30] was a 50-week RCT that examined the bone marrow fat content at 12 and 50-weeks by weight loss of ≤2% and >2% to ≤4.5%. They found that bone marrow fat only decreased in the 2.5-5% weight loss group and increased in the ≤2% weight loss group.

26. Strelitz et al. (2019) Moderate weight change following diabetes diagnosis and 10 year incidence of cardiovascular disease and mortality.
27. Poppitt et al. (2002) Long-term effects of ad libitum low-fat, high-carbohydrate diets on body weight and serum lipids in overweight subjects with metabolic syndrome.
28. Kiddy et al. (1992) Improvement in endocrine and ovarian function during dietary treatment of obese women with polycystic ovary syndrome.
29. Muls et al. (2001) The effects of orlistat on weight and on serum lipids in obese patients with hypercholesterolemia: a randomized, double-blind, placebo-controlled, multicentre study.
30. Spurny et al (2020) Changes in Bone Marrow Fat upon Dietary-Induced Weight Loss.

Discussion

What we found

Our findings show that low weight loss is beneficial across a wide range of health outcomes. We know that 60% of studies (incorporating 87% of participants) showed improvements in health outcomes but we cannot say precisely how many participants had health improvements or the variation in outcomes across the study populations. Our findings are consistent with previous research, which found evidence that less than 5% weight loss has benefits for cardiovascular outcomes, but goes further to show benefits for broader health outcomes. We examined the impact of weight loss by intervention type and found that both lifestyle and pharmacological (including a combination of both) led to improvements in health outcomes.

Outcome-specific findings

Evidence suggests that low weight loss can lead to improvements in health outcomes, including metabolic, cardiovascular, anthropometric, life quality, inflammatory biomarkers, renal and hepatic, psychosocial and behavioural, pulmonary, and ovulatory function; there was no evidence that low level weight loss les to improvement in total mortality or muscle strength.

Of the health outcome categories, mixed results were most often seen for cardiovascular and metabolic markers (where some factors improved and some worsened). These differences could be due to differences in intervention types and length. It could also be that patterns are less clear among people who have low weight loss. For example, the study by Poppitt et al (2002)[27] found that cholesterol outcomes and systolic blood pressure improved, while triglycerides and diastolic blood pressure worsened. They also examined outcomes by ≥3% weight loss and found that nearly all outcomes showed an improvement (but not diastolic blood pressure). This is further supported by results from the Look AHEAD study (Wing et al, 2011) ,[31] showing that weight loss of ≥2 to <5% was associated with improvements in some risk factors, while weight loss ≥5% to <10% led to improvements in all risk factors, and the magnitude increased with increased degree of weight loss (≥10- <15%, and ≥15%).

31. Wing et al. (2011) Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes

Discussion and limitations

Studies with multiple low weight loss categories

Of the seven studies that, that examined multiple low-moderate weight loss categories, we found that there were no differences in five of them. The other two studies found that the health outcomes only improved in the higher weight loss group, compared to the lower weight loss group, as presented in the case studies.[29,30] This could be due to the lower weight loss group including participants who lost a negligible amount of weight (i.e., there may be a threshold of around 2% of body weight).

How our findings build on previous research

Our findings build on previous work, which primarily examined cardiovascular and metabolic improvements.[16-18] We were able to update and extend these findings, by expanding the search strategy and including a larger number of studies. We considered a broader range of health outcomes following low weight loss and we exclusively considered less than 5% body weight loss. For some health outcomes, it remains unclear whether there are benefits of less than 5% body weight loss; for example, muscle strength, total mortality and pulmonary function. The sample sizes for some health outcomes beyond cardiometabolic remain small (e.g., ovulatory function and muscle strength).

Limitations

Our search strategy was comprehensive, with no limitations on countries, health outcomes or publication date, and yielded a high number of records. We used EPPI-Reviewer software to apply an active learning approach, which greatly reduced screening time but resulted in 3215 records being excluded without being screened. It is possible that there are relevant studies that were not included in this review.

We were unable to conduct meta-analysis due to the stratification of the results not allowing for standard comparisons, differences in the reported information and the interventions. We were unable to provide precise numbers and proportions of participants that had health benefits or provide weightings to the results.

Policy implications and conclusions

Policy implications

Our findings suggest that weight loss of less than 5% can lead to health benefits. This shows that low weight loss may have health impacts, despite not reaching the traditional threshold of 5% weight loss.

We found improvements in health outcomes beyond cardiovascular/metabolic, including quality of life and sleep quality, which may be important for reducing some of the wider societal costs of having excess weight, such as loss of productivity and loss of quality adjusted life years.[2]

Although intervention duration and follow up measures from studies in this review were inconsistent, there is evidence that health benefits from weight loss can persist, even when weight regain occurs, but benefits diminish with greater weight regain.[32]

Conclusions

- This review provides evidence that low weight loss is beneficial to participants for a wide range of health outcomes.
- There is clear evidence that there are health benefits from weight loss, but the threshold at which this occurs is not clear. This review provides evidence that lower levels of weight loss can be beneficial and may support a challenge to the traditional 5% threshold.
- This review and previous research suggests that as weight loss increases, health benefits also improve but it will be important to generate more evidence from the UK.
- Given that low weight loss may impact a broad range of health and well-being outcomes, there may wider societal and economic benefits to low weight loss.

32. Hartmann-Boyce (2023) Long-Term Effect of Weight Regain Following Behavioral Weight Management Programs on Cardiometabolic Disease Incidence and Risk: Systematic Review and Meta-Analysis https://doi.org/10.1161/CIRCOUTCOMES.122.009348

NIHR | Policy Research Unit in Obesity

For more information:

s.russell@ucl.ac.uk

NIHR Policy Research Unit in Obesity
Population, Policy and Practice Research and Teaching Department
UCL Great Ormond Street Institute of Child Health
Faculty of Population Health Sciences
30 Guilford Street
London
WC1N 1EH
https://www.ucl.ac.uk/obesity-policy-research-unit/

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Appendix 1. Search strategy and screening criteria

Search Strategy

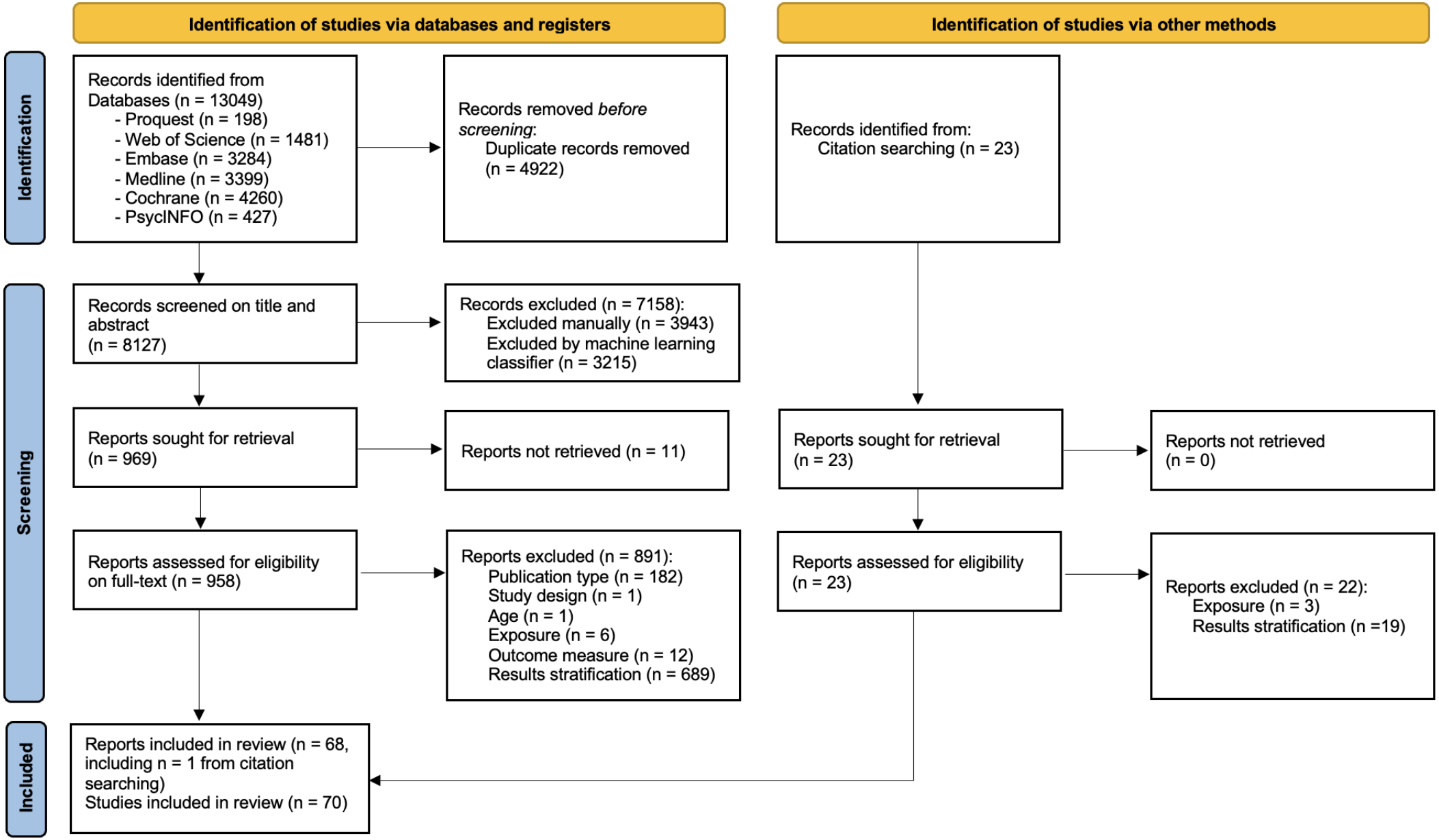
The following main databases were searched (March 2023):

Medline (OVID), Embase (OVID), PsycINFO (OVID), Cochrane Library CENTRAL, Web of Science- social science + emerging sources, ProQuest (Central)- ASSIA.

PICOS framework inclusion and exclusion criteria

	Inclusion	Exclusion
Exposure (intervention)	• Weight loss intervention (lifestyle (physical activity/diet) or pharmacological) • No minimum intervention duration (we will create sub-groups during screening/synthesis)	• Bariatric surgery
Comparison/ study design	Interventional studies including: • Randomized or quasi-randomized controlled trials (RCTs/Q-RCTs) • With pre-post measures	• Uncontrolled studies
Outcome measure – weight loss	• Weight loss of 0-5% from intervention	• Mean weight loss only/ stratified weight loss percentage not reported • No weight loss of 0-5% • We will not contact authors if this is not presented
Outcome measure – health outcomes	Health outcomes assessing benefit of weight loss (not all listed) – that have used a valid/relevant scoring system: • cardiovascular benefits (lipids, BP, glucose) • Other physical health benefits, e.g., mobility; knee pain (e.g., PCS-8); liver function • Sleep Apnoea • Mental health, wellbeing, quality of life, QALYs	No health outcomes of interest measured
Geography **Languages** **Time** **Publication type**	All All No restrictions Peer-reviewed journals	Conference abstracts, reviews, editorials etc.

Appendix 2. PRISMA flowchart



Appendix 3. References – Included studies

1. Abbenhardt, C., et al., *Effects of individual and combined dietary weight loss and exercise interventions in postmenopausal women on adiponectin and leptin levels.* Journal of internal medicine, 2013. **274**(2): p. 163-175.
2. Ahmad, Z., et al., *Weight Change and Its Association with Cardiometabolic Risk Markers in Overweight and Obese Women.* Journal of obesity, 2020. **2020**: p. 3198326.
3. Ahn Shin, Y., et al., *Weight loss has an additive effect on the proteinuria reduction of angiotensin II receptor blockers in hypertensive patients with chronic kidney disease.* Kidney research and clinical practice, 2018. **37**(1): p. 49-58.
4. Alfaris, N., et al., *Effects of a 2-year behavioral weight loss intervention on sleep and mood in obese individuals treated in primary care practice.* Obesity (Silver Spring, Md.), 2015. **23**(3): p. 558-64.
5. Aller, R., et al., *Effect of silymarin plus vitamin E in patients with non-alcoholic fatty liver disease. A randomized clinical pilot study.* European review for medical and pharmacological sciences, 2015. **19**(16): p. 3118-24.
6. Annesi, J.J. and F.A. Stewart, *Contrasts of Initial and Gain Scores in Obesity Treatment-Targeted Psychosocial Variables by Women Participants' Weight Change Patterns Over 2 Years.* FAMILY & COMMUNITY HEALTH, 2023. **46**(1): p. 39-50.
7. Ashley, J.M., et al., *Weight control in the physician's office.* Archives of internal medicine, 2001. **161**(13): p. 1599-604.
8. Bays, H., et al., *Liraglutide 3.0 mg for weight management: weight-loss dependent and independent effects.* Current medical research and opinion, 2017. **33**(2): p. 225-229.
9. Campbell Kristin, L., et al., *Reduced-calorie dietary weight loss, exercise, and sex hormones in postmenopausal women: randomized controlled trial.* Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 2012. **30**(19): p. 2314-26.
10. Chang Hye, M., et al., *Effects of weight reduction on serum vaspin concentrations in obese subjects: modification by insulin resistance.* Obesity (Silver Spring, Md.), 2010. **18**(11): p. 2105-10.
11. Chang, M.-W., et al., *Sleep and weight loss in low-income overweight or obese postpartum women.* BMC obesity, 2019. **6**: p. 12.
12. Christian, J.G., et al., *A Computer Support Program that Helps Clinicians Provide Patients with Metabolic Syndrome Tailored Counseling to Promote Weight Loss.* JOURNAL OF THE AMERICAN DIETETIC ASSOCIATION, 2011. **111**(1): p. 75-83.
13. D'Alonzo Nicholas, J., et al., *WISER Survivor Trial: Combined Effect of Exercise and Weight Loss Interventions on Insulin and Insulin Resistance in Breast Cancer Survivors.* Nutrients, 2021. **13**(9).
14. Davidson Michael, H., et al., *Changes in cardiovascular risk associated with phentermine and topiramate extended-release in participants with comorbidities and a body mass index >=27 kg/m(2).* The American journal of cardiology, 2013. **111**(8): p. 1131-8.
15. Del Ben, M., et al., *Moderate weight loss decreases oxidative stress and increases antioxidant status in patients with metabolic syndrome.* ISRN obesity, 2012. **2012**: p. 960427.
16. Dittus Kim, L., et al., *Impact of a behaviorally-based weight loss intervention on parameters of insulin resistance in breast cancer survivors.* BMC cancer, 2018. **18**(1): p. 351.
17. Dong Tien, S., et al., *The Intestinal Microbiome Predicts Weight Loss on a Calorie-Restricted Diet and Is Associated With Improved Hepatic Steatosis.* Frontiers in nutrition, 2021. **8**: p. 718661.
18. Duggan, C., et al., *Effect of Vitamin D3 Supplementation in Combination with Weight Loss on Inflammatory Biomarkers in Postmenopausal Women: A Randomized Controlled Trial.* Cancer prevention research (Philadelphia, Pa.), 2015. **8**(7): p. 628-35.
19. Duggan, C., et al., *Dietary Weight Loss, Exercise, and Oxidative Stress in Postmenopausal Women: a Randomized Controlled Trial.* Cancer prevention research (Philadelphia, Pa.), 2016. **9**(11): p. 835-843.
20. Falchi Anna, G., et al., *Weight loss and P wave dispersion: a preliminary study.* Obesity research & clinical practice, 2014. **8**(6): p. e614-7.
21. Georgoulis, M., et al., *Dose-response relationship between weight loss and improvements in obstructive sleep apnea severity after a diet/lifestyle interventions: secondary analyses of the "MIMOSA" randomized clinical trial.* Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine, 2022. **18**(5): p. 1251-1261.
22. Gomez-Huelgas, R., et al., *Impact of Intensive Lifestyle Modification on Levels of Adipokines and Inflammatory Biomarkers in Metabolically Healthy Obese Women.* Mediators of inflammation, 2019. **2019**: p. 4165260.
23. Grandi Silva, A., et al., *Effects of weight loss on dynamic hyperinflation in obese women asthmatics.* Journal of applied physiology (Bethesda, Md. : 1985), 2019. **126**(2): p. 413-421.
24. Habermann, N., et al., *No effect of caloric restriction or exercise on radiation repair capacity.* Medicine and science in sports and exercise, 2015. **47**(5): p. 896-904.
25. Harrigan, M., et al., *Randomized Trial Comparing Telephone Versus In-Person Weight Loss Counseling on Body Composition and Circulating Biomarkers in Women Treated for Breast Cancer: the Lifestyle, Exercise, and Nutrition (LEAN) Study.* Journal of clinical oncology, 2016. **34**(7): p. 669-676.
26. Höchsmann, C., et al., *Effects of a 2-Year Primary Care Lifestyle Intervention on Cardiometabolic Risk Factors: a Cluster-Randomized Trial.* Circulation, 2021. **143**(12): p. 1202-1214.
27. Imayama, I., et al., *Effects of a caloric restriction weight loss diet and exercise on inflammatory biomarkers in overweight/obese postmenopausal women: a randomized controlled trial.* Cancer research, 2012. **72**(9): p. 2314-26.
28. Johnson William, D., et al., *Incremental weight loss improves cardiometabolic risk in extremely obese adults.* The American journal of medicine, 2011. **124**(10): p. 931-8.
29. Jouneau, S., et al., *Analysis of body mass index, weight loss and progression of idiopathic pulmonary fibrosis.* Respiratory research, 2020. **21**(1): p. 312.
30. Kaholokula Joseph, K.a., et al., *Sociodemographic, behavioral, and biological variables related to weight loss in native Hawaiians and other Pacific Islanders*. Obesity (Silver Spring, Md.), 2013. **21**(3): p. E196-203.
31. Kiddy, D.S., et al., *Improvement in endocrine and ovarian function during dietary treatment of obese women with polycystic ovary syndrome.* Clinical Endocrinology, 1992. **36**(1): p. 105-111.
32. Kolehmainen, M., et al., *Weight reduction modulates expression of genes involved in extracellular matrix and cell death: the GENOBIN study.* International journal of obesity (2005), 2008. **32**(2): p. 292-303.
33. Kolotkin Ronette, L., et al., *One-year health-related quality of life outcomes in weight loss trial participants: comparison of three measures.* Health and quality of life outcomes, 2009. **7**: p. 53.
34. Konerman Monica, A., et al., *Impact of a structured lifestyle programme on patients with metabolic syndrome complicated by non-alcoholic fatty liver disease.* Alimentary pharmacology & therapeutics, 2019. **49**(3): p. 296-307.

Appendix 3. References – Included studies

35. Kosiborod Mikhail, N., et al., *Semaglutide improves cardiometabolic risk factors in adults with overweight or obesity: STEP 1 and 4 exploratory analyses.* Diabetes, obesity & metabolism, 2023. **25**(2): p. 468-478.
36. Lang, H.-F., et al., *Weight loss increased serum adiponectin but decreased lipid levels in obese subjects whose body mass index was lower than 30 kg/m2.* Nutrition research (New York, N.Y.), 2011. **31**(5): p. 378-86.
37. Magkos, F., et al., *Effect of lorcaserin on glycemic parameters in patients with type 2 diabetes mellitus.* Obesity (Silver Spring, Md.), 2017. **25**(5): p. 842-849.
38. Maruthur, N.M., et al., *Early response to preventive strategies in the Diabetes Prevention Program.* Journal of general internal medicine, 2013. **28**(12): p. 1629-1636.
39. Mason, C., et al., *The effects of separate and combined dietary weight loss and exercise on fasting ghrelin concentrations in overweight and obese women: a randomized controlled trial.* Clinical endocrinology, 2015. **82**(3): p. 369-376.
40. Messier, V., et al., *Effects of the addition of a resistance training programme to a caloric restriction weight loss intervention on psychosocial factors in overweight and obese post-menopausal women: A Montreal Ottawa new emerging team study.* Journal of Sports Sciences, 2010. **28**(1): p. 83-92.
41. Miazgowski, T., et al., *Cardiometabolic health, visceral fat and circulating irisin levels: results from a real-world weight loss study.* Journal of endocrinological investigation, 2021. **44**(6): p. 1243-1252.
42. Muls, E., et al., *The effects of orlistat on weight and on serum lipids in obese patients with hypercholesterolemia: a randomized, double-blind, placebo-controlled, multicentre study.* International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity, 2001. **25**(11): p. 1713-21.
43. Muramoto, A., et al., *Three percent weight reduction is the minimum requirement to improve health hazards in obese and overweight people in Japan.* Obesity research & clinical practice, 2014. **8**(5): p. e466-75.
44. Nadinskaia, M., et al., *Ursodeoxycholic acid as a means of preventing atherosclerosis, steatosis and liver fibrosis in patients with nonalcoholic fatty liver disease.* World journal of gastroenterology, 2021. **27**(10): p. 959-975.
45. Nagahara, M., et al., *[Verification of the effects of three percent weight loss at 6 months and application possibility of assessment at 3 months after the specific health guidance for male workers].* Sangyo eiseigaku zasshi = Journal of occupational health, 2021. **63**(3): p. 86-94.
46. Patrick, D.L., D.M. Bushnell, and M. Rothman, *Performance of two self-report measures for evaluating obesity and weight loss.* OBESITY RESEARCH, 2004. **12**(1): p. 48-57.
47. Perreault, L., et al., *Sex differences in diabetes risk and the effect of intensive lifestyle modification in the Diabetes Prevention Program.* Diabetes care, 2008. **31**(7): p. 1416-21.
48. Poppitt Sally, D., et al., *Long-term effects of ad libitum low-fat, high-carbohydrate diets on body weight and serum lipids in overweight subjects with metabolic syndrome.* The American journal of clinical nutrition, 2002. **75**(1): p. 11-20.
49. Rintamaki, R., et al., *Long-term outcomes of lifestyle intervention to prevent type 2 diabetes in people at high risk in primary health care.* Primary care diabetes, 2021. **15**(3): p. 444-450.
50. Rock Cheryl, L., et al., *Favorable changes in serum estrogens and other biologic factors after weight loss in breast cancer survivors who are overweight or obese.* Clinical breast cancer, 2013. **13**(3): p. 188-95.
51. Rusu, E., et al., *Effects of lifestyle changes including specific dietary intervention and physical activity in the management of patients with chronic hepatitis C--a randomized trial.* Nutrition journal, 2013. **12**: p. 119.
52. Scott, H.A., et al., *Dietary restriction and exercise improve airway inflammation and clinical outcomes in overweight and obese asthma: a randomized trial.* Clinical and experimental allergy : journal of the British Society for Allergy and Clinical Immunology, 2013. **43**(1): p. 36-49.
53. Sharma, A.M., et al., *Blood pressure changes associated with sibutramine and weight management - an analysis from the 6-week lead-in period of the sibutramine cardiovascular outcomes trial (SCOUT).* Diabetes, obesity & metabolism, 2009. **11**(3): p. 239-50.
54. Sheng Jennifer, Y., et al., *The impact of weight loss on physical function and symptoms in overweight or obese breast cancer survivors: results from POWER-remote.* Journal of cancer survivorship : research and practice, 2022. **16**(3): p. 542-551.
55. Shirai, K., et al., *The effects of partial use of formula diet on weight reduction and metabolic variables in obese type 2 diabetic patients - Multicenter trial.* Obesity Research and Clinical Practice, 2013. **7**(1): p. e43-e54.
56. Smith, S.R., et al., *Orlistat 60 mg reduces visceral adipose tissue: a 24-week randomized, placebo-controlled, multicenter trial.* Obesity (Silver Spring, Md.), 2011. **19**(9): p. 1796-1803.
57. Spurny, M., et al., *Changes in Bone Marrow Fat upon Dietary-Induced Weight Loss.* Nutrients, 2020. **12**(5).
58. St George, A., et al., *Effect of a lifestyle intervention in patients with abnormal liver enzymes and metabolic risk factors.* Journal of gastroenterology and hepatology, 2009. **24**(3): p. 399-407.
59. Strelitz, J., et al., *Moderate weight change following diabetes diagnosis and 10 year incidence of cardiovascular disease and mortality.* Diabetologia, 2019. **62**(8): p. 1391-1402.
60. Swift Damon, L., et al., *Effects of aerobic training with and without weight loss on insulin sensitivity and lipids.* PloS one, 2018. **13**(5): p. e0196637.
61. Swift Damon, L., et al., *Effects of clinically significant weight loss with exercise training on insulin resistance and cardiometabolic adaptations.* Obesity (Silver Spring, Md.), 2016. **24**(4): p. 812-9.
62. Thibault, V., et al., *The increase in serum 25-hydroxyvitamin D following weight loss does not contribute to the improvement in insulin sensitivity, insulin secretion and beta-cell function.* The British journal of nutrition, 2015. **114**(2): p. 161-8.
63. Tseng, M.-C., et al., *Psychobehavioral response and weight loss prediction in a hospital-based weight reduction program.* Journal of the Formosan Medical Association = Taiwan yi zhi, 2002. **101**(10): p. 705-11.
64. Vasiljevic, N., et al., *The Relationship Between Weight Loss and Health-related Quality of Life in a Serbian Population.* EUROPEAN EATING DISORDERS REVIEW, 2012. **20**(2): p. 162-168.
65. Vetter, M.L., et al., *Effect of lifestyle intervention on cardiometabolic risk factors: results of the POWER-UP trial.* International journal of obesity (2005), 2013. **37 Suppl 1**: p. S19-24.
66. Wing Rena, R., et al., *Improving urinary incontinence in overweight and obese women through modest weight loss.* Obstetrics and gynecology, 2010. **116**(2 Pt 1): p. 284-292.
67. Wing Rena, R., et al., *Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes.* Diabetes care, 2011. **34**(7): p. 1481-6.
68. Wu, C.-H., et al., *What extent of weight loss can benefit the health-related quality of life in motivated obese Chinese?* Asia Pacific journal of clinical nutrition, 2009. **18**(3): p. 423-32.

Appendix 4 – Bias assessment

Author (Year)	1	2	3	4a	4b	4c	5	6	7	8	9
Abbenhardt (2013)											
Ahmand (2020)											
Ahn (2018)											
Alfaris (2015)											
Aller (2015)											
Ashley (2001)											
Bays (2017)											
Campbell (2012)											
Chang (2010)											
Chang (2019)											
Christian (2011)											
D'Alonzo (2021)											
Davidson (2013)											
Del Bel (2012)											
Dittus (2018)											
Dong (2021)											
Duggan (2015)											
Duggan (2016)											
Falchi (2014)											
Georgoulis (2022)											
Gomez-Huelgas (2019)											
Grandi (2019)											
Habermann (2015)											
Harrigan (2016)											
Höchsmann, (2021)											
Imayama (2012)											
Johnson (2011)											
Jouneau (2020)											
Kaholokula (2013)											
Kiddy (1992)											
Kolehmainen (2008)											
Kolotkin (2009)											

Author (Year)	1	2	3	4a	4b	4c	5	6	7	8	9
Konerman (2019)											
Kosiborod (2022)											
Lang (2011)											
Magkos (2017)											
Maruthur (2013)											
Mason (2015)											
Messier (2009)											
Miazgowski (2021)											
Muls (2001)											
Muramoto (2014)											
Nadinskaia (2021)											
Nagahara (2021)											
Patrick – study 2											
Perreault (2008)											
Poppitt (2002)											
Rock (2013)											
Rusu (2013)											
Scott (2012)											
Sharma (2009)											
Sheng (2022)											
Shirai (2013)											
Smith (2011)											
Spurny (2020)											
St. George (2009)											
Swift (2016)											
Swift (2018)											
Thibault (2015)											
Tseng (2002)											
Vasiljevic (2012)											
Vetter (2013)											
Wing (2010)											
Wing (2011)											
Wu (2009)											

Appendix 4 – Bias assessment

Author (Year)	1	2	3	4	5a	5b	6a	6b	7	8	9	10	11	12
Annessi (2023)									NA					NA
Rintamaki (2021)									NA					NA
Strelitz (2019)									NA					NA