Systematic review of the long-term effects and economic consequences of treatments for obesity and implications for health improvement


CRD summary
This review of obesity treatments in adults concluded that there are beneficial effects of orlistat, sibutramine and metformin and low-fat diets, and that exercise and/or behaviour therapy appear to improve weight loss when added to diet. The review was generally well-conducted and the conclusions are likely to be reliable.

Authors' objectives
To review obesity treatments in adults in order to identify therapies that impact by achieving weight reduction, risk factor modification, or improved clinical outcomes.

The report also included systematic reviews of epidemiological data and of health economic evaluations to address further objectives.

Searching
Thirteen electronic databases were searched to April 2001: MEDLINE, EMBASE, BIOSIS Previews, CAB Nutrition Abstracts and Reviews, the Cochrane Controlled Trials Register, PsycINFO, the Science Citation Index, British Library Inside, CINAHL, HealthSTAR, AMED, SPORTDiscus, UK National Research Register; the search terms were reported. This was supplemented with handsearches of selected journals, including several specific to nutrition and obesity, to June 2001. The reference lists of relevant reviews and RCTs were checked, and companies, experts in the field and authors of relevant abstracts were contacted for further studies. It was unclear whether there were any language restrictions.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials (RCTs) were eligible for inclusion. They were required to have a mean or median duration of at least 52 weeks.

Specific interventions included in the review
Studies of drugs, diets, exercise, behaviour therapy, surgery and complementary therapies specifically aimed to reduce weight, or to prevent weight gain, were eligible for inclusion. Multifaceted interventions (i.e. not solely aimed at weight loss) were excluded. Studies of surgical interventions, complementary medicines, exercise and/or behaviour therapies alone (i.e. without dietary advice) were excluded, as were comparisons between low-fat and low-calorie diets, comparisons of two variations of the same type of diet, and comparisons between low-sodium and weight-loss diets. The drugs examined in the review were limited to orlistat, sibutramine, metformin, acarbose and selective serotonin re-uptake inhibitors (SSRIs).

Participants included in the review
Only studies of adult participants were included (mean or median age of 18 years or older). The mean or median body mass index was required to be at least 28 kg/m2.

Outcomes assessed in the review
To be included in the review, weight loss or the prevention of weight gain had to be explicitly stated as the main study outcome. The primary outcomes sought were weight change and waist circumference, although the main outcome of interest was weight change. Other reported outcomes were also included in the review.

How were decisions on the relevance of primary studies made?
One reviewer assessed titles and abstracts for inclusion, consulting a second reviewer in cases of uncertainty.
Assessment of study quality
Methodological quality was assessed by rating the following features of each study: allocation concealment, handling of withdrawals and drop-outs, and the blinding of participants, health care providers and outcome assessors. One reviewer completed the quality assessment and a second reviewer checked it; neither was blinded to the author, institution or journal. Any disagreements were resolved by discussion, or by referral to a third reviewer if required.

Data extraction
One reviewer extracted the data into a standard form. A second reviewer checked the extraction and any disagreements were resolved by discussion, or by referral to a third reviewer if required. Where only graphical data were available, these were analysed using a computer. Intention-to-treat analyses were used where available. A weighted mean difference (WMD) and 95% confidence interval (CI) were calculated for continuous data, while an odds ratio and 95% CI were calculated for dichotomous data. Where there were multiple comparisons with the same control group, the control group was split for dichotomous data but used more than once for continuous data. Further details of the data transformation and how missing data were imputed were provided.

Methods of synthesis
How were the studies combined?
The studies were grouped by intervention and comparator and were combined by meta-analysis with a fixed-effect model, weighting by the inverse of the variance. Where it was not possible to combine the studies quantitatively, a narrative synthesis was undertaken.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test and I² statistic. Where there was evidence of heterogeneity, possible causes were discussed in the text of the review.

Results of the review
Eighty-four RCTs were included in the review.

Drug interventions: the long-term weight change with orlistat and sibutramine in conjunction with diet was significantly greater than with placebo and diet. The WMD was -3.01 kg (95% CI: -3.48, -2.54) with orlistat at 24 months and 4.12 kg (95% CI: -4.97, -3.26 with sibutramine at 18 months. Blood lipid levels also decreased with both drugs, but only orlistat was associated with a fall in blood-pressure. Metformin and SSRIs were not associated with significant weight loss over 12 months. However the UK Prospective Diabetes Study found metformin to be associated with decreased mortality at 10 years in diabetic participants. There was insufficient evidence on the effects of acarbose.

Dietary interventions: a low-fat or 600 kcal/day diet was associated with a significant weight change, compared with control, at 12 months (WMD -5.31 kg, 95% CI: -5.86, -4.77) and also at 24 and 36 months. It was also associated with the prevention of type 2 diabetes and improved control of hypertension. The protein-sparing modified fast was not shown to have a greater effect on weight than a low-fat or 600 kcal/day diet. There was insufficient evidence to assess the putative benefits of low-calorie or very low-calorie diets.

Exercise and behaviour therapy: the addition of an exercise programme to diet was associated with additional weight change at 12 months (WMD -1.95 kg, 95% CI: -3.22, -0.68), along with improvements in blood lipids. The addition of behaviour therapy to diet was also associated with additional weight change (WMD -7.67 kg, 95% CI: -11.97, -3.36). It was unclear whether the addition of both exercise and behaviour therapy further enhanced weight loss.

Mode of delivery: family therapy was associated with more weight change than individual treatment at 12 months (WMD -2.96 kg, 95% CI: -5.31, -0.60). There was insufficient evidence to assess group versus individual therapy.

Cost information
None. The report included a separate systematic review of economic evaluations.

**Authors' conclusions**
Orlistat and sibutramine appear beneficial for the treatment of adults with obesity, and metformin for obese patients with type 2 diabetes. Exercise and/or behaviour therapy seem to improve weight loss when added to diet. Low-fat diets with exercise, with or without behaviour therapy, are associated with the prevention of type 2 diabetes and hypertension.

**CRD commentary**
The inclusion and exclusion criteria were clearly defined. The search for primary studies was thorough, using a wide range of sources and including searches for unpublished work. It is therefore unlikely that relevant studies were missed, although it was unclear whether or not any language restrictions were applied. The methodological quality of the included studies was assessed and some reference was made to the quality of the individual studies in the text of the review. The quality assessment and data extraction processes were checked by a second reviewer, which should have minimised the introduction of bias and errors at these stages. The studies were grouped and combined appropriately using meta-analysis. Statistical heterogeneity was assessed and, when detected, potential causes were explored. Conclusions were drawn only where there was sufficient evidence. The review was generally well conducted and the conclusions are likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors did not explicitly state any implications for practice in addition to their conclusions. Research: The authors stated that further adequately powered studies are needed in high-risk populations, and that future drug trials should incorporate lifestyle interventions in addition to dietary advice.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.