Treatment of pediatric obesity: a systematic review and meta-analysis of randomized trials


CRD summary
The authors concluded that there was limited evidence that medications and lifestyle interventions reduced paediatric obesity in the short term and that their long-term effectiveness and safety was unclear. The tentative conclusions appear appropriate, given the poor quality and heterogeneity of the primary studies. Potential publication bias in the review increased the need to interpret the evidence cautiously.

Authors' objectives
To assess the effectiveness of non-surgical interventions for treatment of childhood obesity.

Searching
MEDLINE, ERIC, EMBASE, CINAHL, PsycINFO, Dissertation Abstracts, Science Citation Index, Social Sciences Citation Index and Cochrane Central Register of Controlled Trials databases were searched from inception to February 2006. The search strategy was available from the authors. The references of reviews and guidelines were handsearched and experts in the field were consulted. The search was restricted to fully published articles.

Study selection
Randomised controlled trials (RCTs) of non-surgical interventions for obesity in children and adolescents (aged two to 18 years) were eligible for inclusion provided most of the participants were overweight (as defined in the primary study). Studies of lifestyle interventions (aimed at diet and/or physical activity) or pharmacological agents administered to reduce obesity were eligible. Lifestyle interventions could target participants directly or via family, school or community and could be delivered by community members, school staff, family or health care professionals. Studies were required to report an objective mass-based obesity measure at the end of follow up, such as body mass index (BMI) (preferred outcome), percent overweight, recent fat-free mass or visceral adiposity. Studies of participants with insulin resistance or type two diabetes were eligible, but studies of patients with obesity as part of a clinical syndrome (such as type one diabetes, eating disorders and Prader-Willi syndrome) were excluded, as were studies either aiming to reduce cardiovascular risk factors or which reported percent weight loss regardless of height.

Participants in the included studies were adolescents and pre-pubertal children, mostly female, who were recruited by self-referral or from school, community, clinic or in-patient settings. Study inclusion criteria for overweight/obesity varied widely (where reported) with respect to measures and thresholds used (such as skin fold thickness, BMI percentile, weight/height index and subjective diagnosis of parent or physician). Pharmacological interventions in the review included a range of drugs such as sibutramine, orlistat, metformin, sympathomimetics, dehydroepiandrosterone and fibre supplements. Participants in these studies were not required to have tried lifestyle interventions first. Dietary interventions varied. They included reduced glycaemic load, protein-sparing, low-carbohydrate, high-protein and hypocaloric diets. Lifestyle interventions included various physical or dietary programmes and combinations of these. Controls received a wide variety of active or placebo interventions or no intervention. There was wide variation between the studies in the duration of the intervention, which ranged from one month to five years; in most cases the duration of intervention and follow up was no more than six months. Outcomes reported in the review included body mass index in kilograms per square metre (kg/m²), adiposity (percent body fat and fat free mass) and medication side effects.

Teams of two or more reviewers independently selected studies for inclusion. Disagreements were resolved by another reviewer.

Assessment of study quality
The following aspects of study validity were assessed: allocation concealment; nature of blinding; level of randomisation; and extent of losses to follow up. Pairs of reviewers conducted the assessment independently.

Data extraction
Mean differences between the two groups in end-of-study outcomes (preferred measure) or changes from baseline were calculated, with 95% confidence intervals (CIs). Means and estimates of variance were calculated from available data using standard Cochrane Collaboration methods. Outcomes measured within six months of starting the intervention were defined as short-term. Pairs of reviewers independently extracted the data. Attempts were made to contact study authors to confirm data extraction and request missing information.

Methods of synthesis
Data were grouped by comparison (exercise alone versus control, pharmacological therapy versus placebo and combined lifestyle modifications versus control). They were pooled using a random-effects model to calculate standardised mean differences (SMDs), with adjustment for small samples. Effect sizes were defined as small (0.2 or less), moderate (about 0.5) or large (0.8 or more). Heterogeneity was assessed using the $I^2$ statistic, and was defined as small ($I^2$ under 25%), moderate ($I^2$=25% to 50%) and large ($I^2$ over 50%). Subgroup analyses were conducted to investigate the effects of various methodological and clinical characteristics of the included studies.

Results of the review
Approximately 73 RCTs were included, including approximately 61 with data suitable for meta-analysis; however, there was inconsistency in the reporting of study numbers. Sample sizes ranged from 10 to 498 individuals and from 34 to 98 families. Only one RCT clearly reported allocation concealment. Sixteen, all with pharmacological interventions, reported blinding. Nearly half had losses to follow up of 10 per cent or more.

**Pharmacological treatment versus placebo (17 RCTs):** There was a large statistically significant effect favouring sibutramine over placebo (1.01, 95% CI: -1.28 to -0.73; three RCTs) equating to a drop in BMI of 2.4 kg/m$^2$ (95% CI: 1.8 to 3.1) after six months of use. The sibutramine group had higher rates of elevated blood pressure and pulse rate than controls. There was moderate inconsistency between studies ($I^2$=30%). Orlistat was associated with a small to moderate statistically significant effect (-0.29, 95% CI: -0.46 to -0.12; three RCTs) without inconsistency, equating to a drop in BMI of 0.7 kg/m$^2$ (95% CI: -0.3 to 1.2). Gastrointestinal side effects were more common in the orlistat group. Studies of other medications reported no statistically significant findings.

**Lifestyle interventions versus controls (56 RCTs):** RCTs of dietary interventions reported no statistically significant findings (six RCTs). RCTs of physical activity had inconsistent findings: a moderate treatment effect was associated with the intervention when adiposity was the outcome (OR -0.52, 95% CI: -0.73 to -0.30; six RCTs); but findings were not statistically significant when BMI was the outcome (11 RCTs). There was some indication of reporting bias for this finding. Pooling of three RCTs of reduction in sedentary behaviour reported no statistically significant findings. Pooling of 23 RCTs of combined lifestyle interventions showed a small to moderate statistically significant effect favouring the intervention groups; subgroup analyses found that the largest effects were associated with parental involvement in delivering the intervention and that there was a trend towards a larger effect in younger children (aged eight years or younger).

Authors' conclusions
There was limited evidence that medications and lifestyle interventions reduced paediatric obesity in the short term and their long-term effectiveness and safety was unclear.

CRD commentary
The objectives and inclusion criteria of the review were clear. Relevant sources were searched for studies, but the restriction to published studies meant that the review may have been subject to publication bias. It was not clear whether the search was also restricted by language. Relevant criteria were used to assess validity and steps were taken to minimise the risk of bias and error by having more than one reviewer independently undertake study selection, validity assessment and data extraction. There was some inconsistency between the text and tables with respect to the number of included studies. The quality characteristics of individual studies were not reported. Appropriate methods were used to combine the studies statistically and to assess and investigate statistical heterogeneity, but it did not appear that the potential for publication bias was assessed formally. Other potential sources of heterogeneity and bias were well addressed in the discussion section. As the authors noted, the studies were heterogeneous and (in most cases) small, short term and methodologically weak. The authors' tentative conclusions appear appropriate, given the poor quality and heterogeneity of the primary studies. Potential publication bias in the review increases the need to interpret the
evidence cautiously.

Implications of the review for practice and research

**Practice:** The authors stated that paediatric obesity required a careful multidisciplinary and multimodality approach in line with the Endocrine Society practice guidelines.

**Research:** The authors stated that researchers needed to determine the best outcome for measuring the effect of health interventions for obesity in children (for example, BMI or body fat measures). Long-term RCTs were needed to investigate the effectiveness, feasibility and safety of multimodality algorithms for obesity. The long-term clinical effects of interventions such as bariatric surgery and new pharmacological approaches for high-risk children also needed to be assessed.

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