

Pediatric Obesity: Meta-Analysis of Non-Surgical Interventions

In order to inform practice guidelines, the Endocrine Society's Task Force on Pediatric Obesity engaged the Mayo Knowledge and Encounter Research Unit to conduct a meta-analysis of published, randomized trials for pediatric obesity lifestyle and pharmacological interventions.¹ Overweight or obese children aged 2- through 18-years served as participants in the individual studies forming the meta-analysis. Pharmacological interventions included medications aimed at reducing measures of obesity in children (ie, BMI, percent overweight, percent fat-free mass and visceral adiposity). Lifestyle interventions included treatment strategies targeting physical activity and/or dietary changes. Eligible treatments targeted the child, parent, family, school, or community. Interventionists included community agents, school personnel, family members, or healthcare personnel.

Fully published randomized trials were identified through a systematic search of the following databases: MEDLINE, EMBASE, ERIC, CINAHL, Cochrane Central Register of Controlled Trials, PSYCInfo, Dissertation Abstracts International, Science Citation Index, and Social Science Citation Index. Publications through February 2006 were included. Reference sections of reviews and published guidelines were reviewed, and suggestions from experts on The Endocrine Society Pediatric Obesity Task Force were included. From these, 76 articles were considered eligible for the meta-analysis; in all, 61 trials had complete data to include in meta-analyses. Working in pairs, trained reviewers extracted study details and mean or variance data were calculated.

Effect size and 95% confidence interval (CI) for the difference between the intervention and control groups were calculated, as well as standardized mean differences. Subgroup analyses were conducted for degree of parental participation, child age, percent body fat versus BMI, and the combination of reduced sedentary behavior and increased physical activity. Standardized mean differences of about 0.2 or less were considered small, about 0.5 as moderate, and about 0.8 or greater as large effect sizes. The likelihood of between-study variability being attributable to true between-study differences (versus chance) was quantified using the I^2 statistic (inconsistency is considered small when $I^2 < 25\%$, moderate 25%-50%, and large $> 50\%$).

A total of 17 trials of pharmacological interventions formed this portion of the meta-analysis: sibutramine (3 trials)— the pooled effect size, favoring treatment, was large (-1.01 ; CI = -1.8 to -0.73 ; $I^2 = 30\%$) and consistent with a loss in BMI of 2.4 kg/m^2 (CI = 1.8 to 3.1 kg/m^2) after 6 months of use (patients taking sibutramine had higher rates of elevated blood pressure and pulse rate than patients taking placebo); orlistat (3 trials) — the pooled effect size was small to moderate (-0.29 ; CI = -0.46 to -0.12 ; $I^2 = 0\%$) and consistent with a loss in BMI of 0.7 kg/m^2 (CI = 0.3 to 1.2 kg/m^2). More patients

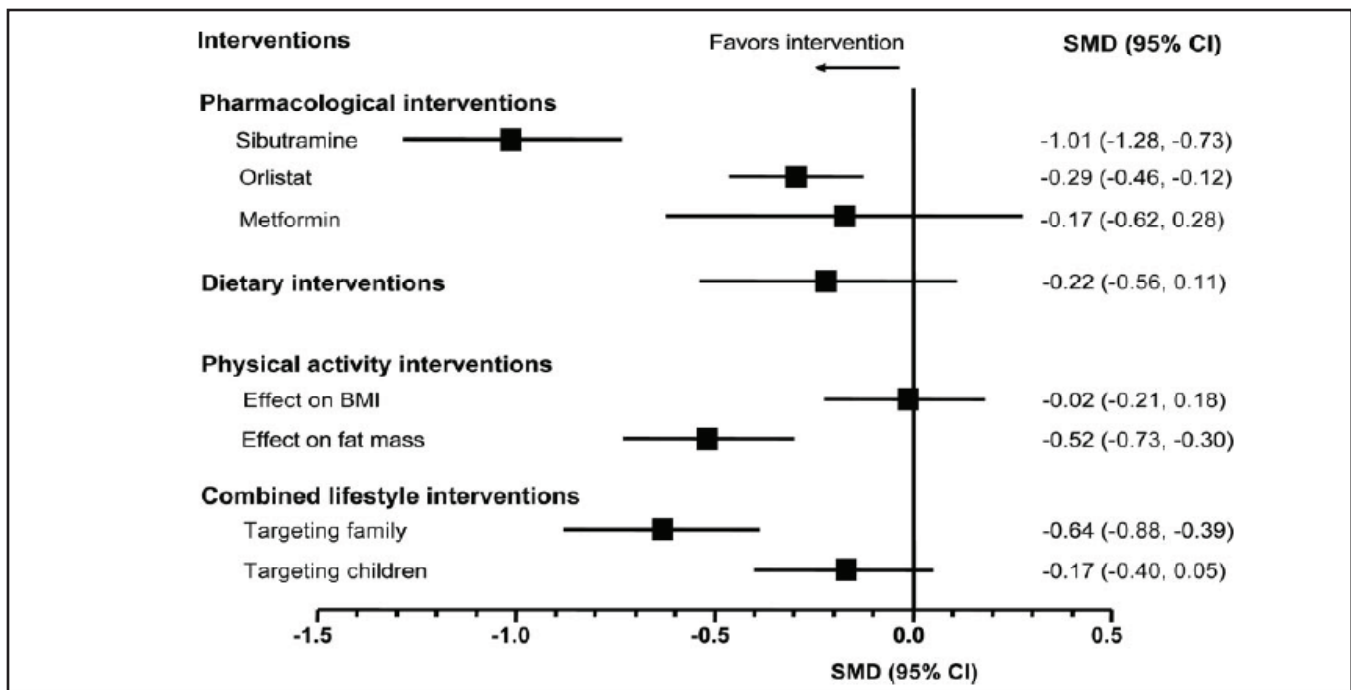
taking orlistat reported GI side effects than patients on placebo; metformin monotherapy for hyperinsulinemic nondiabetic obese adolescents lead to a small nonsignificant change in obesity outcome at 6 months (-0.17 ; CI = 0.62 to 0.28). The remaining trials measured the effect of sympathomimetics (ephedrine and caffeine, dexfenfluramine), dehydroepiandrosterone, and fiber supplements (results reported in figure). Trials of rimonabant in children or adolescents were not identified in the literature.

Lifestyle interventions were divided into “dietary interventions only” (ie, reduced-glycemic-load diet, protein-sparing modified diet, low-carbohydrate diet, high-protein diet, and hypocaloric diet versus control; $n=6$), “physical activity interventions only” ($n=17$), and “combined lifestyle interventions” ($n=23$). The pooled effect sizes and between-study inconsistency for dietary interventions were both small (-0.22 ; CI = -0.056 to 0.11 ; $I^2 = 22.5\%$). Physical activity interventions yielded inconsistent results: the investigators examined whether the choice of obesity outcome measure accounted for this. Trials that measured effects on adiposity found a moderate treatment effect (-0.52 , CI = -0.73 to -0.30 ; $I^2 = 0\%$), whereas trials measuring the effect of physical activity on BMI found no significant effect (-0.02 , CI = -0.21 to 0.18 ; $I^2 = 0\%$).

The pooled estimate across combination lifestyle interventions (physical activity and dietary modification) yielded small to moderate treatment effects. The largest effects were associated with greater parental involvement. There was a nonsignificant interaction between child age and parental involvement, with a trend toward a larger treatment effect for children 8 years or younger (-0.70 ; CI = -1.00 to -0.40).

The authors concluded: (1) short-term efficacy of sibutramine and orlistat on BMI; (2) moderate effect of physical activity on adiposity, but not BMI; and (3) small to moderate effect of combined lifestyle interventions on BMI with a nonsignificant trend favoring those interventions with parental involvement, in particular trials involving younger children. The authors discussed research implications related to drawbacks associated with using BMI as an outcome measure (eg, less responsive to change, requires accuracy and reproducibility in measurement, and misinterprets risk in muscular and short children), and suggested using more responsive outcome measures such as fat-free mass or percent body fat in future studies. The authors also suggested that the Endocrine Society's recommendation for a multidisciplinary and multimodal approach to the treatment of pediatric obesity be studied with long-term randomized trials.

McGovern L, Johnson JN, Paulo R, et al. Treatment of pediatric obesity: A systematic review and meta-analysis of randomized trials. *J Clin Endocr Metab.* 2008;93:4600-4605.



Overall summary of meta-analyses results of randomized trials of treatments for pediatric obesity.

Plot shows meta-analytic estimates (■) and 95% CI (horizontal lines). SMD, standardized mean differences.

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Editors' Comment: The generally dim view of the effectiveness of non-surgical approaches to the management of pediatric obesity may be an important contributing factor to the increasing visibility of bariatric surgery programs. The current meta-analysis provides valuable information for the clinician, clinical and public health researcher with an interest in ensuring that management moves forward in an evidence-based manner. Meta-analysis provides the benefit of increasing the statistical power of small or inconclusive studies and can demonstrate how interventions deliver heterogeneous effectiveness in different settings and in different patients. The benefits do not come without drawbacks, however. Meta-analysis cannot improve the quality of the original studies. Further, aggregation of studies without sufficient attention to the heterogeneity of procedures may result in misleading conclusions.

In the case of the current meta-analysis, there was substantial variability in the procedures adopted across lifestyle intervention trials. These studies varied greatly with respect to duration of the intervention, frequency of sessions, content of dietary, behavioral, and exercise components, training of the interventionists, and measurement. For example, in trials categorized as "combined lifestyle intervention category," some used the Traffic Light Diet, whereas others did not state specifically which nutrition recommendations were offered. Duration of exercise also varied; some interventions held exercise sessions 3-times per week, whereas others only provided exercise education. Furthermore, specification of the specific behavioral strategies employed during treatment to promote

behavior change is not consistently described. Given the high degree of unspecified details across studies, it would be premature to adopt generalizations regarding the value of lifestyle interventions, per se.

Effect sizes of the interventions included in this meta-analysis were estimated in reference to control groups. Not only was there great variability across procedures adopted as interventions, there was also great variability with respect to how control groups were defined. Some researchers chose a no-treatment control group, whereas others altered aspects of the intervention delivered to the treatment group and used this modified intervention as the control group. The strength of findings for any single study may be diminished when the intervention group is compared to a control group that is also offering some form of the intervention, albeit modified. The high degree of variability across interventions, together with highly variable control groups, leads us to question whether a meta-analysis is premature.

Another factor to be considered when interpreting the findings of this meta-analysis includes categorization of the lifestyle interventions. Six studies were designated "dietary interventions only." Closer examination of these reveals that 5 of the 6 studies included behavioral and/or physical activity components in addition to the dietary intervention. Only one study was exclusively dietary.² Similarly, for the 17 studies designated as "physical activity interventions only," 8 also included a dietary and/or behavioral component. Although the focus of the studies in these categories may be primarily dietary or physical activity, the addition of other components may weaken the conclusions that can be drawn from a meta-

analysis that is specifically analyzing “dietary interventions only” or “physical activity interventions only.”

An additional detail regarding studies classified as “combined lifestyle interventions” is noteworthy. The authors suggested a statistically non-significant trend for a larger treatment effect in interventions involving parental involvement in children 8 years of age or younger. This conclusion was based on only 2 studies in which the majority of participants were under age 8 years. Moreover, one of these studies examines a parent-only approach to weight management.³

Given some of our observations, it might be premature to draw firm conclusions about the magnitude of effect sizes of dietary or behavioral interventions and their variability across populations.

The obvious risk would be to make pronouncements that bias future research agenda.

Bethany Sallinen, PhD* and David E. Sandberg, PhD

* Department of Pediatrics and Communicable Diseases and the Division of Child Behavioral Health, University of Michigan, Ann Arbor, Michigan

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Prevention of Pediatric Obesity: Meta-Analysis of Behavioral Interventions

The prevalence of overweight (ie, BMI >95th percentile for age) is currently 16% in children of all ages living in the US. The highest rate occurs among African-American youth. The Endocrine Society’s Task Force on Pediatric Obesity commissioned a meta-analysis of published, randomized trials for interventions aimed at preventing pediatric obesity.¹ In contrast to previous summaries of the literature that focused on the endpoint of body weight, this study sought to summarize the efficacy of interventions aimed at changing lifestyle behaviors, including increased physical activity (PA), decreased sedentary activity (SA), increased healthy dietary habits (HD), and decreased unhealthy dietary habits (UD) to prevent pediatric obesity. In addition, the investigators sought to assess the effect of these interventions on BMI.

Studies eligible for inclusion in the meta-analysis were randomized controlled trials (RCTs) assessing these lifestyle behavior interventions in children or adolescents 2 to 18 years of age. Participants received the interventions at home, school, clinic, or a community setting and healthcare professionals, community members, or health authorities delivered the interventions. Trials with participants who were all overweight or obese were excluded.

Fully published randomized trials were identified through a systematic search of the following databases: MEDLINE, ERIC, EMBASE, CINHALL, PSYCInfo, DISSERTATION abstracts, Science Citation Index, Social Science Citation Index, and the Cochrane CENTRAL database of Controlled Clinical Trials. Publications through February 2006 were included. Reference sections of reviews and expert suggestions were incorporated; 29 trials were considered eligible for the meta-analysis analyzing at least one behavioral endpoint and 34 trials had complete data for BMI. Working in pairs, trained reviewers extracted study details related to the following intervention components: informational (ie, passive information, education), cognitive (ie, general cognitive strategies, goal setting, problem solving/relapse

prevention), behavioral (ie, reminders and prompts for desired behaviors, skill building, practice and rehearsal, monitoring and feedback, and reinforcement of behavior), environmental (ie, physical changes made to change the environment of the school, home, and community), and parental support (ie, active involvement).

An effect size and 95% confidence interval (CI) for the difference between the intervention and control groups were calculated for each of the 4 behavioral targets (ie, increase physical activity, decrease sedentary activity, increase healthy behavior, and reduce unhealthy dietary behavior) and BMI. Standardized mean differences of about 0.2 or less were considered small, about 0.5 as moderate, and about 0.8 or greater as large effect sizes. The likelihood of between-study variability being attributable to true between-study differences (vs chance) was quantified using the I^2 statistic (inconsistency is considered small when I^2 is >25%, moderate 25%-50%, and large >50%). Several preplanned subgroup analyses of RCTs were performed.

Interventions to increase physical activity. Twenty-two randomized trials were included in the meta-analysis to assess the effects of interventions to increase physical activity. Results suggested a small increase in physical activity (effect size = 0.12; CI = 0.4 to 0.20) with moderate inconsistency across trials (I^2 = 63%) which could not be explained by subgroup analyses. There was a trend toward favoring the inclusion of multiple cognitive components (0.15; CI = 0.05 to 0.4; vs 1 or no cognitive components) and reinforcement (0.24; CI = 0.06 to 0.41; vs no reinforcement).

Interventions to decrease sedentary activity. Meta-analysis of 14 RCTs yielded a small reduction of sedentary activity (−0.29; CI = −0.35 to −0.22), with high consistency in results across studies (I^2 = 0%). Several significant treatment x subgroup interactions were detected: treatment effects were greater in trials measuring in-treatment outcomes (−0.32; CI = −0.39 to −0.25; vs outcome measured after treatment), treatment duration >6 months