Pediatric Obesity Interventions in Racial and Ethnic Minorities: A Systematic Review

By

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ABSTRACT

Background: The prevalence of childhood obesity has increased dramatically in the United States, disproportionately afflicting racial and ethnic minorities and producing lifelong health consequences. Various lifestyle and pharmacologic obesity interventions have been analyzed with inadequate representation of minority populations. Systematic reviews that address obesity interventions in minority populations have not been published. Even with the increasing research on pediatric obesity, many clinicians and public health professionals are uncertain of effective interventions in minority populations.

Purpose: To identify pediatric obesity intervention studies in minority populations and assess the effectiveness of these interventions.

Data Sources: The MEDLINE database (inception through February 2008).

Study Selection: The author selected prospective studies of various pediatric obesity interventions with adequate racial and ethnic minority participation that reported an outcome related to body mass index.

Data Extraction: Predefined criteria were used to extract details on study design, study duration, study population, intervention type and outcomes. The studies were then graded as good, fair or poor. The overall body of evidence was then graded as high, moderate or low.

Results: Ten eligible articles were included in the systematic review, seven of which were randomized controlled trials (RCT), one of which was a secondary analysis of an existing RCT, and two of which were prospective cohort studies. African-American and Hispanic children were the most common minority population represented. Five studies were effective in reducing adiposity. Only two studies were graded as good, while many had serious methodological flaws. Moderate evidence exists for some pharmacological interventions in decreasing adiposity, but evidence for lifestyle interventions alone is limited.

Conclusions: Studies that address racial and ethnic minorities are limited. Available evidence does not clearly support any obesity intervention in minority populations, although pharmacotherapy in patients at high risk for comorbidities or combined with lifestyle changes may offer some benefit.
INTRODUCTION

Background

Obesity is a significant public health crisis that affects all ages, racial and ethnic groups. The prevalence of overweight and obesity in children in the United States has increased dramatically over recent years, disproportionately affecting minority groups and contributing to existing racial and ethnic health disparities. According to recent estimates, about 34% of children, ages two to nineteen, are considered overweight or at risk of overweight.\(^1\) Between 1963 and 2000, the prevalence of overweight in children aged six to eleven increased from 4% to 15.3% and from 5% to 15.5% among adolescents in the United States.\(^2\) The prevalence of overweight in adolescents increased in each racial group from 1988 to 2000, according to the National Health and Nutrition Examination Survey (NHANES), with the most significant increase in non-Hispanic blacks (13.4% to 23.6%) and Mexican Americans (13.8%-23.4%).\(^3\) Children ages six to eleven years of age also experienced similar prevalence trends in racial groups.\(^2\) Although overweight and obesity affect all children, the prevalence rose more than twice as fast among minority groups compared with white groups in the United States.\(^4\)

Measurement of Overweight/Obesity

The body mass index (BMI) has been accepted as an indicator for overweight and obesity in children\(^5,\,6\) and is predictive of obesity risk as an adult.\(^7\) BMI has also been shown to correlate with actual body fat in children and adolescents.\(^8,\,9\) One study found that the BMI or the BMI percentile are optimal measures in assessing change in adiposity as a child grows.\(^10\) In 2000, the Centers for Disease Control and Prevention first designated the term, *overweight*, to children,
ages two to eighteen, with a body mass index at or above the 95th percentile for age and sex, and those children with a BMI between the 85th and 95th percentile for age and sex were termed at risk for overweight.\textsuperscript{5,11} This terminology has recently been revised by an expert committee who published recommendations to consider greater than the 95th percentile as obese and between the 85th and 95th percentiles as overweight.\textsuperscript{12} The term obese had not been designated as a weight category in childhood before prior to this change in terminology. This change strengthens the clinical relevance of BMI measurement, is more continuous with adult measures and better reflects the seriousness of associated health consequences.\textsuperscript{12}

Body mass index is commonly used to classify children as overweight or obese, but measuring the change in BMI over time is less straightforward. Researchers have investigated various methods to track change in body mass index and have demonstrated differences in the individual measures.\textsuperscript{13} This is a significant consideration when determining the effectiveness of an intervention based on a single measure. When children are still growing, the absolute change in BMI is not an accurate measure of treatment effect,\textsuperscript{13} and other measures are more informative. However, this may have less influence in BMI monitoring in adolescents since growth has slowed. Obesity intervention studies have analyzed changes in absolute BMI, percent BMI, BMI z-score, BMI centile,\textsuperscript{10} percent over-BMI and BMI sympercent.\textsuperscript{13} One study found that BMI and percent BMI are superior measures, since BMI z-score can get progressively smaller the more obese the child.\textsuperscript{10} Although BMI z-score is still considered a valuable tool to measure overweight in children, the percent over-BMI is recommended in clinical decision making and showing changes in obesity interventions.\textsuperscript{13} Many studies provide more than one measure to better reflect changes in adiposity over time.
Causes

Pediatric obesity is largely caused by an imbalance between energy intake and expenditure with inadequate physical activity and poor nutrition with excess calorie-dense foods. Although studies suggest that genetics may have a significant influence on individual risk, the widespread, dramatic increase in childhood obesity is more likely related to behavior changes and environmental factors than genetic modification. The complex interaction between genes, environment and behavior lead to chronic obesity, which is associated with substantial health consequences that continue throughout one’s life-course.

Racial and ethnic minority children and adolescents are disproportionately affected with higher rates of obesity. Studies have shown that low socioeconomic status is associated with higher rates of overweight and obesity. Urban populations, in particular, appear more susceptible because of poor diet and limited opportunity for physical activity. Current research addressing the causes and associated factors that contribute to obesity are still being investigated, including the possible protective effects of breastfeeding, independent of racial and socioeconomic group.

Health Consequences

A wide array of literature has examined the burden of pediatric obesity, associated health outcomes, the trends in prevalence among different racial and ethnic groups, and options for prevention and treatment of pediatric obesity. Long-term health consequences, in particular, are of significant concern since overweight children have a higher risk of being overweight adolescents and overweight adults. With increasing rates of obesity, Type 2 diabetes is a serious health consequence that has also increased among children. In the United States, studies
have estimated that 8 – 43% of new-onset diabetes cases in the pediatric population are considered Type 2 diabetes mellitus. The SEARCH for Diabetes in Youth Study Group, who intended to provide the most comprehensive data to date on diabetes prevalence in children, found 6379 cases out of about 3.5 million children and adolescents. For youths 10 – 19 years of age, the crude prevalence was 2.80 cases per 1000 youths, while the crude prevalence was less in children aged 0 – 9 years, estimated at 0.79 cases per 1000 children. Minorities, including Native Americans, African-American, Hispanic and Pacific Islander/Asian children, are at higher risk of developing this chronic disorder. For example, 76% of new diabetes cases diagnosed in Native American children aged 12-19 years were identified as Type 2 diabetes mellitus. Children with diabetes are at risk for heart disease, stroke, limb amputations, kidney failure and blindness, all of which are consequences of long-standing diabetes. Other complications of pediatric obesity include sleep apnea, asthma and exercise intolerance, in addition to serious hepatic, renal, musculoskeletal and neurological complications.

Since childhood obesity frequently continues into adulthood, it is a contributor to the adult obesity epidemic and its associated morbidity and mortality. As in adults, obesity in childhood is associated with increased incidence of cardiovascular disease risk factors, such as hypertension, dyslipidemia, chronic inflammation, increased blood clotting tendency, endothelial dysfunction and hyperinsulinemia. These complications are considered components of the insulin resistance syndrome (IRS), which has been identified in children as young as age five. The metabolic effects of the insulin resistance syndrome may differ by race or ethnicity. Caucasian children were shown to have significantly more visceral fat, which is associated with IRS, when compared to African-American children. However, independent of visceral fat, African-American children were shown to be more insulin resistant. These differences
require more research to better understand the influence of racial and ethnic disparities in pediatric overweight and obesity, as well as illustrate the importance of effective obesity interventions in minority children to prevent harmful health outcomes.

Overweight and obese children or adolescents may also experience psychological problems such as negative self-esteem, withdrawal from peer interaction, depression, anxiety and the feeling of chronic rejection, as well as significantly lower quality of life. Obese adolescents with lower self-esteem were also shown to have higher rates of loneliness, sadness, nervousness, as well as an increased risk of smoking and drinking alcohol. In addition, obese Hispanic and white females were shown to develop significantly lower self-esteem by early adolescence than those who were not obese. The extensive multi-system health consequences associated with pediatric obesity require effective prevention and treatment interventions in childhood, as well as life-long management.

**Additional research needed**

Although obesity prevention is crucial, a significant number of children are already overweight or obese and experience health consequences as a result. The complexity and difficulty of managing childhood obesity and its complications, such as type 2 diabetes mellitus, leave many primary care providers uncomfortable with treatment options. Additionally, primary care providers often lack the time and resources to offer intensive interventions and have few opportunities for referral. As a result, providers and the public health community are in need of evidence-based interventions that are effective in addressing pediatric obesity. Some studies aim to provide guidance and recommendations for managing pediatric obesity, but few address racial, ethnic or cultural concerns associated with this health problem. Many existing
studies assess intervention effects on homogeneous populations. Even with the increasing amount of literature regarding pediatric obesity interventions, disparities continue to widen with higher prevalence in Mexican-American boys and African-American girls.\textsuperscript{1} Considering overweight interventions have been shown to be less effective in minority populations than in whites,\textsuperscript{45} or studies fail to include adequate representation of different racial and ethnic groups, effective interventions that are sure to include all racial or ethnic groups are necessary to prevent growing disparities. Therefore, the aim of this paper is to conduct a systematic review examining the effectiveness of interventions in childhood overweight and obesity in racial and ethnic minorities.
METHODS

Inclusion Criteria

The goal of this systematic review was to identify interventions designed for childhood overweight and obesity and assess their effectiveness in minority populations. The purpose is to determine if specific interventions will work in populations other than Caucasian/white, and not compared to this population. Types of interventions in this review include: pharmacologic treatment, surgical treatment, lifestyle changes (dietary, physical activity, behavioral) or a combined therapy. Studies can assess effects by comparing the intervention to another treatment or to no intervention. Clinical, community or school-based interventions were included and there was no restriction on who was delivering the intervention.

Randomized controlled trials were included in the review if they analyzed an intervention of at least 12 weeks in duration. Observational studies were included if they had at least 50 participants and the intervention was at least 6 months in duration.

No comparison between racial or ethnic groups was required. No limit was placed on how many racial/ethnic groups were addressed in a particular study and one group was considered sufficient. To assess these interventions in minority populations, studies that only address minorities as a specific objective or identified minorities in the study were included for review. If a study did not focus on a specific minority group, then the baseline characteristics should have reflected at least 40% of the study participants in a racial or ethnic group other than Caucasian or white. There was no standard cut-off determined for adequate minority representation, so this percentage was arbitrarily chosen to be more than population representation, but less than majority since a majority may have narrowed results dramatically
due to the under-representation of minorities in research studies. African-American, Hispanic, Asian, Alaska native/Native American, or Other, were possible racial/ethnic categories to identify study participants, although African-American and Hispanic participants were more commonly included. Since this review focuses on treatment and not on prevention, the study must have enrolled overweight or obese participants at baseline, with a BMI > 85% for age and gender. However, articles were not excluded if normal-weight children also participated. All children under age 18 at the start of the study were included in this review.

To be included in the review, the study must have assessed some outcome of weight, including baseline and post-intervention height and weight, body mass index (BMI), BMI percentile change or BMI z-score.

**Exclusion Criteria**

Studies were excluded from the review if they did not meet the predetermined inclusion criteria outlined above. Studies that included children with chronic diseases (other than Type II diabetes mellitus), psychiatric co-morbidities or children taking a medication that affects weight control (i.e. anti-psychotics or corticosteroids) were excluded. Studies that included participants with Type II diabetes were not excluded since this condition is often associated with obesity and can lie on a continuum for severely obese youth may already have aspects of the metabolic syndrome prior to developing diabetes. These participants especially are in critical need of effective interventions for obesity to help treat the condition, although obesity interventions prior to this point of health consequences are preferable. Any study that dealt with eating disorders (anorexia nervosa, bulimia) was also excluded, as well as studies that dealt with weight control
for pregnant females. In addition, organic or syndromal causes of obesity, such as the genetic syndrome, Prader-Willi, were excluded from this review.

Table 1: Eligibility Criteria

<table>
<thead>
<tr>
<th>Study design</th>
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<tr>
<td>• Randomized controlled trial $\geq$ 12 week intervention OR</td>
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<td>• Observational studies with at least 50 participants and duration $\geq$ 6 months.</td>
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<tr>
<th>Study population</th>
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<tr>
<td>• Overweight or obese* children, ages 0-18. Did not exclude articles that contained normal weight participants, as long a majority of overweight or obese participants were included.</td>
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<tr>
<td>• Article addresses specific minority group OR includes $\geq$ 40 % racial/ethnic minority group (African-American, Hispanic, Asian, Native American, etc.)</td>
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<tr>
<td>• Children with BMI $&lt; 85^{th}$ percentile accepted if separate analysis than those with $\geq 85^{th}$ percentile</td>
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<tr>
<th>Study intervention</th>
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<tr>
<td>• Any clinical or community intervention, including behavioral, pharmacotherapy, surgical, etc.</td>
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<th>Outcome measure</th>
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<tr>
<td>• Body mass index (BMI)</td>
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<tr>
<td>• BMI percent change</td>
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<tr>
<td>• BMI z-score</td>
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* The terms, *overweight* and *obese*, are used to reflect the most recent recommendations in terminology\textsuperscript{12} and includes children with a BMI $\geq 85^{th}$ and $\geq 95^{th}$ percentile respectively. Studies may identify these participants as *at risk for overweight* and *overweight*, but still refer to a BMI $\geq 85^{th}$ percentile or $\geq 95^{th}$ percentile.
Literature Search Strategy

In order to find articles that addressed the key question, I performed a MEDLINE electronic database search, using PubMed, from inception through February, 2008. All searches were limited to children, ages 0-18, to concentrate on the pediatric population, and articles in the English language. The search strategy began with the MeSH term, “overweight” or “obesity,” although the latter term should be included in the first term. Both terms were used at first, but the remaining searches utilized “overweight” since it better reflected the terminology used in much of the pediatric literature since a BMI > 95th percentile was considered “overweight” until recently, yielding a more sensitive search. To find studies on treatment or intervention, the subheading, “therapy” was used in conjunction with “overweight.” This primary search for overweight yielded 4708 articles. To focus on minority population interventions, I searched “African-Americans” and “Hispanic” MeSH terms. The search for overweight therapy was combined with the search for African-American or Hispanics, yielding 132 articles. In order to include articles that may include the general term, “minorities,” a search for overweight therapy and minorities was used and yielded 61 articles. A final search included overweight therapy and African-American or Hispanic populations or overweight therapy and minority populations, yielding a total of 177 articles. Of these, 29 articles were randomized controlled trials (using clinical queries). I conducted a title review of all 177 articles and found 99 applicable articles. I excluded 98 articles that clearly were not relevant to the topic or addressed a topic included in the exclusion criteria. I conducted an abstract review of the 99 articles, followed by a full article review of 28 articles.

In addition to articles that explicitly addressed minority populations, I searched for general childhood overweight articles that enrolled participants of different races and ethnicities.
A search for overweight therapy for children, ages 0-18, again yielded 4708 articles. From these, I limited the search to 447 randomized controlled trials. I conducted a title review and excluded 328 articles that did not address the key question, included adults, or clearly contained one or more of the exclusion criteria. I then conducted an abstract review of the remaining 119 articles, followed by a full article review of 40 articles (overlap with the previously reviewed 28 articles).

I also hand-searched the reference lists of background articles for potentially relevant studies that may have been missed with the search strategy. The search was repeated multiple times from the start to ensure reproducibility and strength of the search strategy.
Figure 1: Article Selection

Search results
N = 4708

African-Americans, Hispanics or minorities
N = 177

Title review
Excluded 78 articles (no intervention of interest, use of exclusion criteria or did not address key question)

Abstract Review
N = 99

Excluded 71 articles
Failed to meet inclusion criteria

Full text review
N = 28

Excluded 58 articles
Failed to meet inclusion criteria (short duration, too few participants for observational study, inadequate minority participation)

Randomized Controlled Trials
N = 447

Title review
Excluded 328 articles (included adults, contained exclusion criteria or did not address key question)

Abstract Review
N = 119

Excluded 79 articles
Failed to meet inclusion criteria/ adequate minority population

Full text review
N = 40

Articles selected for review
N = 10

Hand search
N = 1
Data Extraction and Quality Assessment

I extracted data from each study in the review, including characteristics of participants (number of participants, racial/ethnic group, age range, baseline BMI, etc), type of intervention (clinical, school-based, community), magnitude of effect/outcomes, adverse events, study design and quality of study. To assess internal validity of randomized controlled trials, I used predefined criteria used by the U.S. Preventive Services Task Force to grade each study as good, fair or poor.\textsuperscript{46} For example, these guidelines consider the following characteristics of a randomized controlled trial: comparable groups with adequate randomization and concealment of allocation; maintenance of comparable groups throughout the study; differential or high loss to follow-up; equal, reliable and valid measurement; clear definition of intervention and appropriate analysis. The internal validity and quality of observational studies were assessed by the criteria summarized by Deeks et al.\textsuperscript{47} External validity is discussed, but did not affect the quality rating. Additional information on the grading criteria is found in Appendix A.

Data Synthesis

Since the interventions varied widely and some focused on a specific racial or ethnic group alone, I will concentrate on a qualitative synthesis by describing each study, results and limitations, rather than performing a quantitative analysis.

Rating of the Overall Strength of Evidence

Overall strength of the evidence was rated as very low, low, moderate or high, as shown in Table 2. The ratings are based on the definitions and recommendations outlined in the GRADE Working Group paper,\textsuperscript{48} which incorporates the following key elements to guide the
quality review: study design, study quality, consistency and directness. This approach provides a systematic way of grading the quality of evidence and remains consistent with other systematic reviews. The grade reflects the strength of the body of evidence for the efficacy of the different types of pediatric obesity interventions. Directness was not addressed in this review since all potential articles were required to address the effectiveness of an intervention with predetermined outcome measures and were therefore considered direct.

Table 2. Definitions in grading the overall quality of evidence

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
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<tbody>
<tr>
<td>High</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td>Low</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td>
</tr>
<tr>
<td>Very Low</td>
<td>Any estimate of effect is very uncertain.</td>
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</table>

Source: Grade Working Group48
RESULTS

Using the search strategy outlined in the methods section, ten studies were identified that met the inclusion criteria. All eligible studies were included independent of quality, but are assessed based on the pre-established quality criteria. Seven studies were randomized controlled trials, one study was a secondary analysis of an existing randomized controlled trial and two were observational studies. Studies addressed various age ranges with an overall span of age eight to eighteen. All studies looked at interventions in racial and ethnic minorities, and most commonly focused on African-Americans and Hispanics. Four studies focused on one particular racial/ethnic group alone, two of which concentrated on African-American females and two on Hispanic youth. Participant characteristics of included studies are summarized in Table 2.

There were a variety of interventions offered in the included studies. Six studies included a behavioral intervention that promoted changes in eating and physical activity habits, three studies examined the effects of pharmacotherapy and two studies investigated the combination of a behavioral intervention with pharmacotherapy. All randomized controlled trials offered at least the standard of care to the control group. No surgical intervention studies were found that met the inclusion criteria for racial and ethnic minority participation.

Of the four studies that evaluated pharmacotherapy, two were funded by pharmaceutical companies, one was funded by research grants and one was not reported.
Table 3: Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Author Year</th>
<th>Mean BMI (kg/m²) % overweight or obese*</th>
<th>Participants</th>
<th>Age, years</th>
</tr>
</thead>
</table>
| Berkowitz et al 2006 | 100% obese (≥ 2 units above 95th percentile) | N = 498
56.0% White (n = 206)
21.7% African-American (n = 80)
16.3% Hispanic (n = 60)
6.0% Other (n = 22) | 12 – 16 |
| Budd et al 2007      | 100% overweight/obese                  | N = 82
54.9% White (n = 45)
41.5% African-American (n = 34)
1.2% Hispanic (n = 1)†
2.4% Other (n = 2)† | 13 – 17 |
| Ebbeling et al 2006  | 44% overweight                         | N = 103
35.9% White (n = 37)
64.1% Non-white (n = 66)
17.5% Hispanic (n = 18) | 13 – 18 |
| García-Morales et al 2006 | 100% obese              | N = 46
100% Hispanic | 14 – 18 |
| Germann et al 2006   | 100% obese                            | N = 150
88% African-American (n = 132)
6% Hispanic (n = 9)
6% Other (n = 9) | 8 – 18 |
| Johnston et al 2007  | 100% overweight/obese                 | N = 60
100% Hispanic | 10 – 14 |
| Resnicow et al 2000  | 100% overweight/obese                 | N=57
100% African-American | 11 – 17 |
| Savoye et al 2007    | 100% obese                            | N = 174 ‡
36.8% white (n = 64)
38.5% African-American (n = 67)
24.7% Hispanic (n = 43) | 8 – 16 |
| Srinivasan et al 2006 | 100% obese               | N = 28
25% White (n = 7)
64% Non-white (n = 18)
11% Mixed background (n = 3) | 9 – 18 |
| Williamson et al 2006 | 100% overweight/obese            | N = 57
100% African-American | 11 – 15 |

*Overweight defined as a BMI ≥ 85th percentile and obese defined as a BMI ≥ 95th percentile.
† Due to the small n, these participants were excluded from the secondary analysis.
‡ 209 participants originally randomized, but structured meal plan group (n = 35) discontinued due to the high dropout rate (83%).
Studies Examining Pharmacotherapy Interventions

Two randomized controlled trials,\textsuperscript{52,57} assessed the effects of pharmacotherapy compared to placebo in obese participants, summarized in Table 3. Both studies only enrolled those children who were considered obese, with a body mass index equal or greater than the 95\textsuperscript{th} percentile for age and gender and were referred to an endocrine clinic. One study\textsuperscript{52} found no significant difference between placebo and pharmacotherapy, whereas the other study\textsuperscript{57} found pharmacotherapy to be significantly better than placebo. One of the RCTs compared placebo with sibutramine (Meridia\textsuperscript{®}), a serotonin and norepinephrine reuptake inhibitor that has been shown to aid in weight loss and weight maintenance in obese adults,\textsuperscript{59-61} and has been the subject of investigation in obese adolescents.\textsuperscript{49,62} The other RCT studied the effects of metformin, a drug that is used in the treatment of Type II diabetes mellitus and can benefit youth with this chronic condition.\textsuperscript{63} The role of metformin in weight loss and insulin sensitivity prior to the development of Type II diabetes has been analyzed in adults,\textsuperscript{64} and increasingly in adolescents.\textsuperscript{57,65-69} However, only two identified articles utilizing metformin for weight control included a sufficient number of minority participants,\textsuperscript{57,67} one of which met inclusion criteria for this systematic review. Although the objective in both studies was to assess the effects of pharmacotherapy and not lifestyle changes, both trials offered information on healthy eating habits and physical activity but did not measure the effects.

García-Morales et al randomized 51 obese Mexican children to a trial of sibutramine 10mg daily or placebo for 6 months. However, only 46 children were included in the analysis since 5 participants dropped out early (3 treatment, 2 placebo). The study finished with a 90-100\% compliance rate, and had a 24\% non-differential dropout rate, with 11 children withdrawing (5 from sibutramine group, 6 from placebo group). In addition to sibutramine or
placebo, all subjects were given individualized dietary and physical activity advice. The investigators assessed the safety of sibutramine use in adolescents and reported a small number of adverse events, including elevated blood pressure and heart rate, headache, dry mouth, nausea, weakness and paleness. None of the side effects warranted discontinuation. Although both groups experienced clinically significant weight loss, the difference between the sibutramine and placebo group was not statistically significant. The study by García-Morales et al was rated fair due to the high post-randomization exclusions (11%) and the lack of a true intent-to-treat analysis.

Srinivasan et al randomized 28 participants in a 12-month cross-over study to receive metformin, 1 g twice daily, vs. placebo for 6 months each, after a two-week wash-out period. Although this review only focuses on the effects of treatment on anthropometric measures, this study assessed insulin sensitivity and safety of sibutramine as well. The study population was at higher risk of obesity complications, as reflected by acanthosis nigricans in 89% of participants, a clinical feature of insulin resistance. After 6 months of treatment, those subjects receiving metformin showed a significant beneficial effect over placebo in weight, weight z-score, BMI, BMI z-score and waist circumference, as well as a benefit in fasting insulin and a small benefit in fasting glucose. The change in insulin sensitivity was not significant between groups, a finding that the authors associated possibly to the inadequate loss of visceral fat. Only 2 younger participants were not able to tolerate metformin 1 g twice daily due to nausea, but did well with 750mg twice daily. Median adherence for both groups was 78%, which may reflect real-life compliance with treatment. The drop-out rate was 14.3%. This study by Srinivasan et al was rated good without serious methodological flaws.
Table 4. Summary of Pharmacotherapy Interventions

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Study design/ [N]/ Study duration</th>
<th>Intervention</th>
<th>Outcome measure</th>
<th>Results</th>
<th>Quality Rating</th>
</tr>
</thead>
</table>
| García-Morales et al, 2006 | RCT 46 6 months | Sibutramine 10mg daily vs. placebo | Body weight, BMI and %BMI | *Sibutramine*  
Weight: –7.3kg [95% CI –4.6 to -9.9]  
BMI: –3.2 kg/m² [–2.3 to –4.1 kg/m²]  
%BMI: –9.2 [–6.9 to –11.6]  
*Placebo*  
Weight: –4.3kg [95% CI –1.7 to –6.9]  
BMI: –2.0 kg/m² [–0.9 to –3.0 kg/m²]  
%BMI: –5.2 [–2.4 to –7.9]  
P > 0.05 | Fair |
| Srinivasan et al, 2006 | RCT, crossover 28 6 months | Metformin 1g twice daily vs. placebo | Weight, BMI, BMI z-score, body composition, insulin sensitivity | *Difference (metformin vs. placebo)*:  
Weight: – 4.35 kg  
BMI: – 1.26 kg/m²  
BMI z-score: – 0.12 | Good |

Studies Examining Behavioral Interventions

The majority of the reviewed literature examined behavioral interventions, focusing on diet, physical activity and nutrition education. Six studies assessed behavioral interventions that focused on lifestyle changes, four of which were randomized controlled trials. Results are summarized in Table 4. All except one study focused on children or adolescents who were already overweight or obese, with a body mass index of at least the 85th percentile for age and gender. Five of the studies were intensive lifestyle interventions and one study
focused only on a specific behavioral modification. Two of the intensive lifestyle interventions were family-based, one of which utilized the internet to deliver the intervention.

The least intensive intervention focused on decreasing sugar-sweetened beverages in the diet to bring about weight loss and found no overall significant difference in the effect on BMI. Ebbeling et al randomized a diverse group of 103 adolescents (47 males and 56 females) who regularly drank sugar-sweetened beverages to an intervention group that received weekly home delivery of non-caloric beverages for 25 weeks vs. a control group that continued usual beverage intake behavior. Baseline characteristics of the participants were compared using gender, race, ethnicity, age, household income, household size, weight, height and body mass index (BMI), and did not differ except that the intervention group was slightly heavier. In addition, they did not differ in baseline daily intake of sugar-sweetened or non-caloric beverage intake, physical activity, television viewing or total media time. The subjects received enough beverages for the household and could choose which types of drinks, such as bottled water or “diet” drinks (soft drinks, ice tea, lemonade, punch, etc). Subjects also received advice on beverage selection when they were away from home. The investigators examined the change in sugar-sweetened beverage consumption, as well as BMI. No other measure of BMI was reported to compensate for growth, but participants were adolescents, ages 13-18. Participants were asked to recall dietary intake and physical activity with random telephone surveys. Although these interviews relied on recall and may be subject to bias, the adolescents participated in group training sessions to learn how to estimate portion sizes and measure intensity of physical activity. This study had a 100% completion rate and the consumption of sugar-sweetened beverages decreased by 82% in the intervention group. Although no overall significant difference in BMI was found, they considered the baseline BMI to be an effect modifier and found a significant change in BMI in
those subjects with higher BMI’s to start. Therefore, the investigators concluded that this intervention could decrease sugar-sweetened beverage consumption and may have a beneficial effect on body weight and BMI with increasing body weight. The investigators blinded the phone interviewers, but did not report if those measuring BMI outcomes were blinded. In addition, without blinding of the participants and the reliance on recall, the subjects could be pressured to provide expected results during the phone interviews. Strengths of this article were the relatively simple intervention and the 100% completion rate, not seen in any of the other studies.

The studies by Germann et al, Resnicow et al, Williamson et al, Johnston et al, and Savoye et al, were similar in that they provided a multi-disciplinary intensive behavioral intervention that focused on healthy eating habits and increasing physical activity, the mainstay of weight loss. As expected with intensive interventions, the drop-out rate was much higher. Three of the studies had a 40% or greater drop-out or loss to follow-up rate,\textsuperscript{53, 55, 56} whereas one study had a 95% completion rate.\textsuperscript{54} One study\textsuperscript{53} had only 23% of participants achieve clinically significant weight loss and another study\textsuperscript{55} demonstrated increased weight and BMI after the intervention. Three studies had positive results, one of which\textsuperscript{54} showed a significant decrease in weight, BMI and standardized BMI over control, another study\textsuperscript{56} showed a significant decrease in BMI and percent body fat over the control group and the last study\textsuperscript{58} found significant percent body fat loss at 6 months but not at 2 years.

Germann et al provided cognitive-behavioral therapy, nutritional education, medical monitoring and structured exercise training as part of the program, \textit{FitMatters}, to a group of 150 low-income minority children (ages 8-18) for one year, 23% of whom achieved weight loss. Of these initial participants, only eighty-three (55%) were able to participate in the follow-up study.
to assess weight loss at an average of 23 months after the initial assessment. This study took a more psychological approach by conducting an initial psychological assessment on each family, providing cognitive-behavioral techniques, such as self-monitoring, stimulus control, anxiety management, coping and relapse prevention, and measuring the following outcomes: consistency of child and parent self-monitoring, behavioral and emotional stability and the degree of perceived familial conflict. Weight control behaviors, exercise levels and eating behaviors were also noted. Studying correlates of success may provide guidance in the design or implementation of a particular intervention. The participants, non-participants and comparison group had similar baseline measures in socioeconomic status, age, ethnicity, initial BMI, intellectual functioning or child and parental self-monitoring. The comparison group was used to look at the rate of weight gain before and after participating, but the comparison group may have differed from those participants for whom previous records did not exist. The investigators designated a change of – 0.70 in BMI z-score as the cutoff for “clinically meaningful weight change,” which nineteen participants (23%) achieved, and compared these “successful” participants with “less successful” participants. Those who were successful in achieving meaningful weight change were observed to participate in more sessions over a longer period of time, be slightly heavier before the program and have better weight control skills. However, these results should be interpreted cautiously. This study was rated poor due to the overall high loss-to-follow-up (44.7%), lack of comparison group, potential differences between those participants that were lost-to-follow-up and their risk of obesity, unequal time of follow-up among participants with no mention of adjusting for individual length of follow-up and no mention of blinding of the outcome assessors.
Like the previous study by Germann et al, Resnicow et al took a social cognitive theory approach to a 6-month intensive intervention in severely obese African-American females but did not demonstrate any improvement in BMI. The study observed 57 youth recruited from inner-city public housing developments. The participants received dietary and exercise guidance, focused mainly on increasing fruit and vegetable intake, decreasing fat intake, decreasing fast food intake, decreasing television viewing and increasing physical activity. The program also worked to reinforce a positive and healthy outlook, decrease negative expectations, and increase confidence in their abilities to change lifestyle, including hands-on cooking experience. On average, the participants attended 43% of the sessions. The investigators compared high and low attendees but found no significant difference in BMI and both groups showed an increase in body weight and BMI. This study was rated poor due to the high overall loss-to-follow-up (45%), little adjustment for confounding and potential selection bias and use of high and low attendees as comparison groups, which may have important differences.

Williamson et al also concentrated on weight loss in African-American females, but rather than a community-based program like the previous study, the investigators evaluated an internet-based lifestyle intervention for 2 years. A slight benefit in percent body fat was demonstrated in the intervention group at 6 months without changes in BMI, but groups were no different at 2 years. Fifty-seven participants were randomized to an interactive internet weight loss program or to a passive internet-based health education program as the control. The girls had to have an overweight parent who was willing to participate in the study. The intervention included interactive nutrition education, counseling and behavior medication through the internet and email, focusing on eating habits and physical activity, in addition to four in-person counseling sessions during the first 12 weeks. The control group differed in that no counseling
or recommended behavioral changes were offered, but only nutrition and exercise education. The intervention group had a significant decrease in the percent body fat in the first 6 months, but did not significantly differ at 2 years. Average body mass index increased slightly for both groups, but to a lesser extent in the treatment group. The more long-term follow-up is a strength of this study with weight maintenance implications. This study was rated poor due to the high overall loss-to-follow-up (30%), lack of information on randomization scheme and baseline characteristics of study participants and no blinding of outcome assessors.

Johnston et al evaluated a culturally-appropriate, intensive behavioral intervention in Mexican-American children in Houston, Texas and found significant decreases in weight, BMI and standardized BMI when compared to the self-help group. After recruitment, 60 children were randomized to receive a school-based, instructor-led intervention (n = 40) vs. a self-help, parent-guided manual, *Trim Kids*, as a placebo (n = 20). Each group was in a separate classroom during the school day. The intervention included 3 months of daily sessions (1 indoor nutrition lesson, 4 outdoor physical activity lesions), followed by 3 months of biweekly sessions. In addition, parents were invited to monthly meetings to learn about healthy eating and family meal planning. To assess adherence to the intervention, participants took biweekly quizzes and wore heart rate monitors to ensure adequate exercise intensity. The investigators attempted to individualize the intervention by modifying participant preferences and using preferred physical activities, in addition to providing all materials in both English and Spanish. This study was rated fair without serious methodological flaws, but it did not report blinding of outcome assessors.

The study by Savoye et al was the largest of all the behavioral interventions and randomized 209 obese children to a family-based, intensive weight management intervention
(n=140), *Bright Bodies*, vs. traditional clinical counseling every 6 months as a control (n=69) and found a significant decrease in BMI. The intervention arm was additionally randomized to receive a structured meal plan (n=35) or learn how to make better food choices (n=105), the former of which was discontinued because of a high drop-out rate (83%) at 6 months. The participating children and their caregivers met together twice a week for 6 months, then twice a month for 6 months, to receive exercise and nutrition. Behavioral modification sessions were also included, with children and caregivers separated, and concentrated on self-awareness, goal setting, stimulus control, coping skills training, cognitive behavior strategies and contingency management. At 12 months, the weight management group had a significant decrease in BMI and percent body fat compared to the control group, as well as significant differences in fasting insulin and insulin sensitivity. The study was only powered to allow for a 20% drop-out rate. This study was rated as poor due to the high overall drop-out rate (47%), high post-randomization exclusions from discontinued arm (17%) and unknown blinding of outcome assessors.
Table 5. Summary of Behavioral Interventions

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Study design/ [N]/ Study Duration</th>
<th>Intervention</th>
<th>Outcome measure</th>
<th>Results</th>
<th>Quality Rating</th>
</tr>
</thead>
</table>
| Ebbeling et al, 2006  | RCT 103 25 weeks                  | Home delivery of non-caloric beverages/ instructed not to drink sugar-sweetened beverages | BMI (adjusted for age and gender)                                                | Intervention group BMI: 0.07 ± 0.14 kg/m²  
Control group BMI: 0.21 ± 0.15 kg/m²  
Among upper baseline-BMI tertile: Intervention BMI: −0.63 ± 0.23 kg/m²  
Control BMI: +0.12 ± 0.26 kg/m²  
Net effect: BMI: −0.75 ± 0.34 kg/m² | Good            |
| Germann et al, 2006   | Prospective cohort study 150 1 year | FitMatters - includes cognitive-behavioral therapy, nutritional counseling, exercise therapy, and medical management | Body weight, BMI z-score                                                        | Mean BMI z-score change: -0.05, SD = 1.41  
23% achieved clinically meaningful weight change, defined as -0.70 z-scores or better. | Poor           |
| Johnston et al, 2007  | RCT 60 6 months                   | Behavioral intervention I: self-help parent-guided manual (Trim Kids) vs. II: instructor-led intervention with daily followed by biweekly sessions | BMI z-score                                                                     | Intervention (II) Weight: −1.75 ± 10.34 kg  
BMI: −1.16 ± 4.17 kg/m²  
%BMI: −2.81 ± 4.42  
Control (I) Weight: +1.31 ± 1.53 kg  
BMI: +0.29 ± 0.51 kg/m²  
%BMI: +0.02 ± 1.69 | Fair            |
<p>| Resnicow et al, 2000  | Prospective cohort study          | Nutritional and physical activity                                            | BMI, % body fat, DXA,                                                           | No significant difference when comparing high and                                           | Poor           |</p>
<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Duration</th>
<th>Intervention Description</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Savoye et al, 2007&lt;sup&gt;56&lt;/sup&gt;</td>
<td>57</td>
<td>6 months</td>
<td>Bright Bodies Family-based intensive lifestyle intervention</td>
<td>Body weight, BMI, % body fat</td>
<td>Intervention: Weight: 0.3kg (-1.4 to 2.0) BMI: – 1.7 kg/m² (-2.3 to -1.1) Control: Weight: 7.7kg (5.3 to 10.0) BMI: 1.6 kg/m² (0.8 to 2.3)</td>
</tr>
<tr>
<td>Williamson et al, 2006&lt;sup&gt;58&lt;/sup&gt;</td>
<td>57</td>
<td>2 years</td>
<td>Interactive behavioral internet program (intervention) vs. internet health education program (control)</td>
<td>Body weight, BMI, body composition and weight loss behaviors</td>
<td>Treatment: BMI +0.73 ± 0.66, %BMI – 0.004 ± 0.003 Control: BMI +1.2 ± 0.65, %BMI – 0.001 ± 0.003 Significant difference in % body fat at 6 mths, not 2 years.</td>
</tr>
</tbody>
</table>

**Studies Examining Combination of Pharmacotherapy and Behavioral Interventions**

One randomized controlled trial<sup>49</sup> and one secondary analysis<sup>50</sup> of a previously published randomized controlled trial<sup>62</sup> investigated the combination of pharmacotherapy with behavioral interventions in diverse populations. Both studies used sibutramine (Meridia®) in conjunction with lifestyle changes to achieve expected optimal results in obese adolescents and found a significant decrease in BMI over placebo. The study by Berkowitz was the largest of all the included articles, enrolling 498 participants from 33 outpatient centers throughout the United States. The behavioral intervention in this study was site-specific, varying across study...
participants, whereas the behavioral program used in Budd et al was the same family-based weight loss program. Both studies used sibutramine 10 mg daily, although one study allowed for an increase to 15 mg if BMI was not reduced by 10% in 6 months, which occurred in 47.9% of participants. The trials also measured adverse events to evaluate the safety of sibutramine use in adolescents.

The 2006 study by Berkowitz et al looked at severely obese participants with a body mass index of at least two units more than the 95th percentile for age and sex. The randomized controlled trial was conducted over one year, with a 3:1 randomization to site-specific behavioral therapy and sibutramine vs. placebo. All participants received behavioral treatment instruction that was designed by the specific center. These instructions included patient-centered lifestyle modifications, such as healthy eating and physical activity counseling, self monitoring, stress management, stimulus control, problem solving, contingency management, cognitive restructuring and social support. The behavioral therapy and sibutramine group significantly decreased BMI when compared to behavioral therapy and placebo, as well as produced larger improvements in percent weight loss, waist circumference, triglyceride levels, high-density lipoprotein (HDL) cholesterol levels, insulin levels and insulin sensitivity. The study only measured BMI and did not include any other measure, such as percent BMI or BMI z-score. Children included in the study were ages 12-16 and could still be growing, which would make BMI measurements less useful. However, the use of waist circumference is useful in assessing adiposity loss, especially visceral adiposity. The overall completion rate was only 72%, although the estimated sample size allowed for a 50% drop-out rate with the expected treatment effects. The placebo group had a greater drop-out rate than the sibutramine group (62% vs. 76%). Due to the differential loss-to-follow-up, this article was rated fair. However, the rate of tachycardia
with sibutramine was significantly more than in the placebo group and adverse events led to withdrawal in 6.3% of the treatment group and 5.4% of the placebo group.

Budd et al performed a subset analysis (n = 79 out of N = 82 in the overall RCT) of a randomized controlled trial published elsewhere, in which 34 African American and 45 Caucasian children with a mean age of 14.1 years were randomized to a family-based behavioral intervention and sibutramine or family-based behavioral intervention and placebo. The original article by Berkowitz et al (2003), which assessed behavioral therapy and sibutramine vs. placebo in a diverse sample, assessed change in percent BMI and BMI z-scores between the treatment and control groups for the first 6 months, and then transitioned to open-label treatment of sibutramine for the entire sample. Adherence to lifestyle program and hunger was measured, as well as blood pressure and pulse for safety measure. Unlike the other pharmacotherapy trials, this study enrolled children who were overweight or obese, with a body mass index of at least the 85th percentile. The sibutramine group significantly lost a greater percentage BMI than the placebo group and the difference in BMI z-score was statistically significant. During the 12 months, nineteen participants experienced elevations in blood pressure and pulse significant enough to warrant reductions, five of which discontinued treatment. Two participants experienced ventricular premature complexes, although one case was not thought to be medication-related. However, this study does raise safety concerns of sibutramine use in adolescents. This original article by Berkowitz et al (2003) was rated good.

Racial and ethnic groups were not evenly distributed in the original analysis, so Budd et al compared weight loss and metabolic risk factors in African-American and Caucasian adolescents as a secondary analysis. No differences in initial BMI or BMI z-score were found comparing African-American and Caucasian adolescents, but larger waist circumferences, higher
triglycerides and higher cholesterol levels were found in the Caucasian group at baseline. Retention did not differ between the two racial groups. In Caucasians, the sibutramine group experienced a larger percent BMI change at 6 months than the African-American sibutramine group. The percent BMI change in the African American group was not statistically significant between sibutramine and placebo groups, but investigators thought this could have been due to the smaller sample size of African Americans. The percent change in BMI was not significantly different between the Caucasian and African American placebo and sibutramine groups. Both racial groups had significant decreases in metabolic risk factors. However, these results should be interpreted cautiously since the original study was not powered for subset analysis, resulting in a fair rating. Overall, the 14% of patients discontinued treatment due to adverse events.

Table 6. Summary of Pharmacotherapy/Behavioral Interventions

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Study design/ [N]/ Study Duration</th>
<th>Intervention</th>
<th>Outcome measure</th>
<th>Results</th>
<th>Quality Rating</th>
</tr>
</thead>
</table>
| Berkowitz et al, 2006<sup>49</sup> | RCT 498 1 year | Behavior therapy + sibutramine vs. behavioral therapy + placebo | BMI, Body weight, waist circum., fasting lipid and glycemic variables, safety, tolerability | *Sibutramine*  
Weight: –6.5kg ± 0.3kg  
BMI: –2.9 kg/m<sup>2</sup> [95% CI –3.5 to –2.2 kg/m<sup>2</sup>]  
*Placebo*  
Weight: +1.9 ± 0.56 kg  
BMI: –0.3 kg/m<sup>2</sup> [95% CI –0.4 to –0.2 kg/m<sup>2</sup>]  
Difference, BMI: –2.6 kg/m<sup>2</sup> [95% CI –3.1 to –2.0 kg/m<sup>2</sup>]  
P < 0.001 | Fair |
Budd et al, 2007 50

RCT (secondary analysis)
82
6 months

Family-based behavioral therapy + placebo vs. Family-based behavioral therapy + sibutramine

Body weight, BMI, % BMI, fasting glucose, insulin, insulin resistance, lipid levels

Overall*
Mean change %BMI:
BT† + Sibutramine: – 8.5 (SD 6.8)
BT + Placebo: – 4.0 (SD 5.4)
Mean change in BMI z-score:
BT + Sibutramine: – 0.2 (0.2)
BT + Placebo: – 0.1 (0.1)

Sibutramine
African-Americans
Weight: – 6.9 ± 6.2 kg
BMI: – 2.9 ± 2.7 kg/m²

Caucasians
Weight: – 9.0 ± 6.4 kg
BMI: – 3.6 ± 2.5 kg/m²

Placebo
African-Americans
Weight: – 3.4 ± 6.8 kg
BMI: – 1.4 ± 2.0 kg/m²

Caucasians
Weight: – 3.0 ± 5.9 kg
BMI: – 1.6 ± 2.1 kg/m²

* Results from original article
† Behavior therapy

Good (original article)/ Fair

**General Efficacy**

In general, five studies49, 50, 54, 56, 57 were shown to be effective in reducing body mass index, percent BMI or BMI z-score, while four studies52, 53, 55, 58 were ineffective in reducing
these measures. One study\textsuperscript{51} was shown to be effective only in those children who were in the upper baseline-BMI tertile, but not for the sample as a whole. However, this was also the only study that included children who were not overweight or obese. The overall strength of the evidence for each intervention is summarized in Tables 7, 8 and 9.
### Overall Strength of Evidence

**Table 7. Evidence Profile for Pharmacotherapy options for treatment of childhood obesity**

<table>
<thead>
<tr>
<th>No. of studies/Patients</th>
<th>Study Design</th>
<th>Study Quality</th>
<th>Consistency</th>
<th>Comments</th>
<th>Summary of findings</th>
<th>Overall Grade of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 / 46 patients</td>
<td>RCT</td>
<td>Fair</td>
<td>N/A</td>
<td>None</td>
<td>No significant difference</td>
<td>Low</td>
</tr>
<tr>
<td>1 / 28 patients</td>
<td>RCT</td>
<td>Good</td>
<td>N/A</td>
<td>Small sample size, limited external validity</td>
<td>Metformin showed benefit over placebo</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

**Table 8. Evidence Profile for Behavioral treatments of childhood obesity**

Evidence profile: Comparative efficacy of behavioral interventions

<table>
<thead>
<tr>
<th>No. of studies/Patients</th>
<th>Study Design</th>
<th>Study Quality</th>
<th>Consistency</th>
<th>Comments</th>
<th>Summary of findings</th>
<th>Overall Grade of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease in Sugar-Sweetened Beverages vs. Maintain current habits Outcome: BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No overall difference</td>
<td>Moderate</td>
</tr>
<tr>
<td>1 / 103 patients</td>
<td>RCT</td>
<td>Good</td>
<td>N/A</td>
<td>Included non-overweight children</td>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td>Internet-based interactive intervention vs. internet-based education Outcome: BMI, %BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No difference in BMI at 6 or 12 months</td>
<td>Low</td>
</tr>
<tr>
<td>1 / 57 patients</td>
<td>RCT</td>
<td>Poor / serious methodological problems</td>
<td>N/A</td>
<td>Slight benefit in percent body fat at 6 months</td>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>Intensive lifestyle intervention Outcome: BMI, BMI z-score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 RCTs showed significant difference</td>
<td>Low</td>
</tr>
<tr>
<td>4 / 476 patients</td>
<td>2 obs. studies, 2 RCTs</td>
<td>2 poor quality with serious methodological problems and 2 fair quality</td>
<td>Some inconsistencies</td>
<td>None</td>
<td></td>
<td>Low</td>
</tr>
</tbody>
</table>
Table 9. Evidence Profile for Combined Behavioral and Pharmacotherapy Treatments of Childhood Obesity

| Evidence profile: Comparative efficacy of combined behavioral/pharmacotherapy interventions |
|---------------------------------|---------------------------------|-----------------|----------------|-----------------|
| No. of studies/Patients         | Study Design | Study Quality | Consistency | Comments | Summary of findings | Overall Grade of Evidence |
| Behavioral intervention + sibutamine vs. placebo | Outcome: BMI, %BMI, BMI z-score | 2 / 580 patients | RCTs | Fair | No inconsistencies | None | Significant decrease in BMI over placebo | Moderate |
DISCUSSION

Childhood and adolescent obesity is an epidemic, disproportionately affecting minority populations and exposing youth to irreversible cardiovascular complications. Much research has been done to identify interventions that are effective in treating obesity, but results of this review show that there is deficient evidence and few high quality studies on pediatric obesity interventions in minority populations. Several studies were not considered for this review because of lacking minority representation, a critical aspect in current obesity research considering the existing disparities.

Of the included studies, many were limited due to small sample size or high attrition rates. Although decreased compliance and drop-outs might be expected in intensive behavioral interventions and increase external validity of these studies by reflecting reality, the internal validity is still limited and the efficacy of the intervention unclear. Most studies had a short duration, with few interventions evaluating the effects beyond six months. The one study that had a follow-up of two years showed no treatment difference.

All pharmacotherapy studies offered some type of lifestyle counseling, whether or not it was included in the measures. These studies showed a beneficial effect of sibutramine or metformin over placebo, but the external validity is limited. Children who would be offered pharmacotherapy would most likely be severely obese and be referred to a specialty clinic, since primary care physicians may not be comfortable prescribing experimental medications. These individuals would have to be involved in the health care system to receive this opportunity. Even with a prescription or a referral to a specialty clinic, weight-loss medications like sibutramine are expensive and often not covered by insurance.\textsuperscript{70}
The use of pharmacotherapy in children should also be carefully weighed against possible harms. The Food and Drug Administration has approved sibutramine in adolescents of 16 years or older, and use under the age of 16 is considered experimental.\textsuperscript{71} Although pharmacotherapy in conjunction with lifestyle changes has shown a beneficial effect over lifestyle changes alone, the effect size is modest. Significant adverse events were documented in all pharmacologic treatments, some leading to discontinuation. Individuals for whom pharmacologic treatment is appropriate should be under careful observation and monitoring. Lifestyle changes should remain first-line treatment, reserving medication use for individuals who have failed behavioral interventions or are at high risk for metabolic comorbidities and cardiovascular complications.\textsuperscript{72}

**Limitations**

Although this review was done systematically, it still has specific limitations. One person conducted the literature search, article selection and grading of the evidence. In order to make up for this limitation, the process was written with full disclosure so that the reader can make his or her own assessment should it differ from the author. Secondly, the review concentrated on diverse populations or specific minority groups to assess interventions in the group that disproportionately carries the burden. Generalizing among groups is a potential limitation of the studies themselves that contributed to the lack of strength of the evidence. Specific differences between Hispanics and African Americans or between two children of the same race may exist, such as socioeconomic status, education and family history, which interfere with a child’s ability to lose weight. The articles attempted to control for these factors but other unknown confounders may still be present.
Included studies may be limited due to selection bias. Many studies relied on recruitment for study enrollment. Participants who enroll could be different from those who decide not to enroll in a study. In addition, they may be more motivated to lose weight in general, which could lessen the treatment effect if both intervention and control groups were more likely to lose weight. On the other hand, studies could suffer from high drop-out or non-compliance rates if participants were not as willing to be involved in the study.

Future Research

As this review highlighted, more research of diverse populations is needed to assess interventions in all children. The vast amount of literature of pediatric obesity is impressive, but only ten articles could be found that included a sufficient number of minorities. Many of the studies were limited by small sample sizes, short-term follow-up or large drop-out rates. Large randomized controlled trials that include children from all backgrounds should be conducted in each type of intervention, especially behavioral interventions. The research community should evaluate a standard intervention in different populations- varied racial/ ethnic groups, rural or urban, low or high-income, less educated, etc- to gain information on generalizability. Intensive interventions may be difficult to maintain participation and can have high drop-out rates. Perhaps assessing the readiness of pediatric patients to change and offering these interventions to highly motivated individuals could increase a study’s validity and efficacy, although limit external validity. In addition, long-term follow-up is critical to assess maintenance of weight loss and resulting benefits.

Important points for future research not addressed in this review are the effects of interventions in preventing or delaying the metabolic effects of insulin resistance and Type II
diabetes, in addition to its effects on body composition. Some studies have analyzed the metabolic effects, especially of pharmacotherapy, and perhaps this could be the subject of future studies in minority populations or a future systematic review.

Although cost-effectiveness was not addressed in this review, its role in future research is significant considering the lifelong health consequences and cardiovascular risks initiated by childhood obesity are considered an epidemic problem and public health emergency. These studies would be difficult to perform, but considering the amount of resources the health care system puts into cardiovascular disease, evidence of effective obesity interventions in children could possibly prevent or delay complications and prove cost-effective. An article on short-term cost-effectiveness in the method of delivering an intervention has been published, but does not take into account the cost of lasting health consequences. Another study estimated costs about $200 a year for overweight or obese children, which could cover 4 visits to a dietician per year. To receive any short-term return of investment, all costs from the child’s overweight or obesity would have to be eliminated. However, considering the lifelong costs of obesity, long-term cost-effectiveness is possible with childhood obesity interventions. Although studies on cost-effectiveness are helpful, the quality of childhood obesity interventions should not be based on financial incentive, but rather efficient weight loss and an increase in quality of life and longevity.

Future interventions should be designed with specific ethnic or cultural considerations that will not exclude children of different backgrounds. All children should have equal opportunity to obesity treatments. Segregation of interventions by population or by racial/ethnic group may prevent exposing the root causes of obesity and addressing these issues, even if an intervention may be more effective in certain populations. Although prevention was not
addressed in this systematic review, additional research on the prevention of childhood obesity and potential risk factors to target early intervention are needed.

The obesity epidemic in children and adolescents has left pediatric providers searching for effective treatments for their patients. Much of the literature does not provide answers as few studies have taken place in the primary care setting.\textsuperscript{75} Outside of community- or family-based interventions, clinical interventions tend to recruit patients from endocrine or specialty obesity clinics. Although these patients are in critical need of intervention, these results are not generalizable to the general population, in addition to limiting interventions to those children without access to the health care system and referrals to specialty clinics. No one intervention is likely to solve the problem of pediatric obesity, but the diverse backgrounds of afflicted children, as well as disparities across racial and ethnic groups, warrant a combined public health approach that targets the individual, the family and the community.
References:


64. Desilets AR, Dhakal-Karki S, Dunican KC. Role of Metformin for Weight Management in Patients Without Type 2 Diabetes (June). *Ann Pharmacother.* May 13 2008.


Appendix A. Quality Assessment Methods

Internal Validity (criteria used by U.S. Preventive Services Task Force)

Controlled Trials:
- Comparable groups
  - Adequate randomization (sequence generation, computer-generated, etc)
  - Allocation concealment (concealed randomization, centralized randomization, etc)
  - Groups similar at baseline, equally at risk
- Eligibility criteria specified
- Maintenance of comparable groups
  - Attrition
  - Crossovers
  - Adherence
  - Contamination
- Loss-to-follow-up
  - Overall high loss-to-follow-up
  - Differential loss-to-follow-up
- Measurements
  - Equal, reliable, valid
  - Blinding of outcome assessors to treatment allocation
- Clear definition of intervention
- Important outcomes considered
- Analysis
  - Intention-to-treat
  - Post-randomization exclusions

Observational Studies: (Deeks, et al)
- Same source population for both groups?
- Same risk of developing outcome at baseline (i.e. obesity)?
- Subjects recruited over same time period?
- Obvious selection bias?
- Ascertainment methods adequate and equally applied?
- Attempt to blind outcome assessors?
- Equal follow-up time period?
- Overall attrition high (> 20%)?
- Differential attrition high (> 15%)?
- Attempt to control for potential confounders in statistical analysis or different lengths of follow-up?
- Adequate length of follow-up?

External Validity

- Similarity of study population to general population deserving of intervention?
• Recruited patients?
• Exclusion criteria?
• Funding source and role of funder?
• Did control group receive standard of care?
• Length of follow-up?
### APPENDIX B. EVIDENCE TABLES

| STUDY | Author: Berkowitz et al\textsuperscript{49}  
Year: 2006 |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>FUNDING:</td>
<td>Abbott Pharmaceuticals (makers of sibutramine)</td>
</tr>
<tr>
<td>RESEARCH OBJECTIVE:</td>
<td>To see if sibutramine increased weight loss more than placebo in obese adolescents who were also receiving behavioral therapy.</td>
</tr>
<tr>
<td>METHODS:</td>
<td>12 month intervention with follow up at month 6 and 12. Weekly visits for first 2 weeks, bimonthly visits until week 12, and month visits after. Participant, investigators and statisticians blinded.</td>
</tr>
<tr>
<td>PARTICIPANTS:</td>
<td>N = 498, ages 12 – 16 years, BMI at least 2 units greater than 95th percentile based on age and sex. Subjects from 33 U.S. outpatient centers 3:1 randomization, n= 368 to sibutramine, n= 130 to placebo</td>
</tr>
<tr>
<td>INTERVENTION:</td>
<td>Instruction in center-specific behavioral program (nutritional counseling, self-monitoring of eating habits and physical activity, stress management, stimulus control, contingency management, cognitive restructuring, social support, dietary and physical activity counseling) + randomization to 10mg sibutramine or placebo. If subject did not lose more than 10% of initial BMI by month 6, then sibutramine or placebo was increased to 15mg.</td>
</tr>
</tbody>
</table>
| OUTCOME ASSESSMENT: | Primary: change from baseline BMI  
Secondary: percentage change in BMI, proportion of patients achieving BMI reductions of 5% or more or 10% or more, absolute and percentage changes in body weight and lipid and glycemic variables, change in waist circumference. Safety assessments: reported adverse events, changes in blood pressure and pulse rate, electrocardiographic variables. Also measured growth (height) and sexual maturation (Tanner staging). |
| RESULTS: | The estimated mean treatment group difference (after 12 months) for change in BMI was – 2.9 kg/m2 [95% CI, -3.5 to -2.2 kg/m2] and body weight – 8.4 kg [95% CI, -9.7 to -7.2 kg]. P < 0.001 for both. Sibutramine group also had significant improvements in triglyceride levels, HDL levels, insulin levels and insulin sensitivity (P < 0.001). Tachycardia was greater for sibutramine (12.5% vs. 6.2% placebo). |
| ADVERSE EVENTS: | Tachycardia more common in sibutramine group than placebo. Other AE’s (with difference in rates of more than 1 percentage pt) were dry mouth, constipation, dizziness. Hypertension caused withdrawal of 5 treatment group participants (0 placebo). 10/368 sibutramine and 1/130 placebo reported serious AE’s, including nausea, vomiting |
ADHERENCE/COMPLIANCE: Assessed by pill count. 89.1% mean adherence in sibutramine group and 83.9% in placebo group.

ANALYSIS: ITT:* modified (defined as all participants who received at least 1 dose of study medication and recorded at least 1 post-baseline BMI). Last-observation-carried-forward with mixed linear effects model. Post-randomization exclusions: None reported

ADEQUATE RANDOMIZATION: Yes

ADEQUATE ALLOCATION CONCEALMENT: Yes

BLINDING OF OUTCOMES ASSESSORS: Yes

ATTRITION: Overall: 72%
Treatment-specific: 76% in sibutramine group vs. 62% in placebo group (P = 0.001)

NOTES AE’s not pre-specified

QUALITY RATING Fair

*ITT = intention-to-treat

STUDY

Author: Berkowitz et al, 200362 (original article)
Budd et al50 (secondary analysis)

Year: 2007

FUNDING: Knoll Pharmaceuticals/ Abbott Laboratories

RESEARCH OBJECTIVE: To examine and compare changes in weight loss and cardiometabolic risk factors in African American and Caucasian adolescents with familial-based behavioral therapy + sibutramine or placebo.

METHODS:

PARTICIPANTS: N = 82 randomized; 79 in secondary analysis; ages 13 – 17 years; BMI ≥ 85th percentile (mean BMI 37.8 kg/m2); from March 1999 to August 2002 at university-based clinic.

INTERVENTION: 6 month intervention of sibutramine + family-based behavioral therapy vs. placebo + same behavioral therapy, then open-label sibutramine treatment for all participants until month 12.

OUTCOME ASSESSMENT: Primary: weight, BMI, BMI z-scores, % change in BMI Secondary: blood pressure, pulse, hunger

RESULTS:

<table>
<thead>
<tr>
<th></th>
<th>Sibutramine + BT</th>
<th>Placebo + BT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>− 7.8 kg (SD 6.3)</td>
<td>− 3.2 kg (SD 6.1)</td>
</tr>
<tr>
<td>% BMI</td>
<td>− 8.5% (SD 6.8%)</td>
<td>− 4.0% (SD 5.4)</td>
</tr>
<tr>
<td>BMI z-score</td>
<td>− 0.2 (0.2)</td>
<td>− 0.1 (0.1)</td>
</tr>
</tbody>
</table>

ADVERSE Pre-defined: Elevations in BP, pulse
### EVENTS:
- 1 patient with ventricular premature complexes (VPCs) (continued 6 months after sibutramine discontinued, thought benign)
- 1 patient with VPCs at 9 months, 3 weeks after sibutramine discontinued, gone at 12 months. Both asymptomatic. During 12 months, sibutramine reduced to 10mg in 16 subjects, 5 mg in 7 additional subjects, and discontinued in 10 participants. 19/43 experienced significant elevations of BP and pulse that led to reductions, and discontinuation in 5 patients.

### ADHERENCE/COMPLIANCE:
Pill count: treatment group used 79.1% of prescribed pills and control group used 78.3% of prescribed pills.

### ANALYSIS:
- ITT: Yes
- Post-randomization exclusions: No

### ADEQUATE RANDOMIZATION:
Randomization scheme not described, small baseline differences in gender and race

### ADEQUATE ALLOCATION CONCEALMENT:
Yes

### BLINDING OF OUTCOMES ASSESSORS:
Yes

### ATTRITION:
- At 6 months: 8 (5 placebo, 3 treatment)
- At 12 months: 20 (10 placebo, 10 treatment)

### NOTES:
- Statistical difference in BMI z-score, but maybe not clinically meaningful. Absolute difference small. BMI decreased additional 2.4% in control group once switched to open-label treatment from months 7-12.

### QUALITY RATING
Good (original article) / Fair (Budd)

* Behavior Therapy

### STUDY
**Author:** Ebbeling et al
**Year:** 2006

### FUNDING:
Grants, National Institute of Diabetes and Digestive Kidney Diseases, Charles H. Hood Foundation and National Institutes of Health

### RESEARCH OBJECTIVE:
To examine the effects of decreasing sugar-sweetened beverages on body weight

### METHODS:
Blinded randomization, stratified by gender and BMI. Telephone contact in first week and then monthly to discuss beverage consumption and provide motivational counseling. Provided in-person training to estimate food/beverage consumption and describe physical activity intensity. Baseline BMI considered an effect modifier (p = 0.016).

### PARTICIPANTS:
N = 103 randomized (47 males, 56 females), ages 13 – 18 years,
who reported consuming at least 1 serving of sugary beverage per day. Excluded those who were currently dieting, cigarette smokers or BMI less than 25th percentile.

**INTERVENTION:** 25 weeks of home delivery of non-caloric beverages of choice based on household size and instructions not to consume sugar-sweetened beverages. Control group asked to continue usual beverage consumption habits.

**OUTCOME ASSESSMENT:** Primary end points: change in body mass index (BMI) Primary process measure: change in consumption of sugar-sweetened beverages

**RESULTS:** Intervention group: consumption of sugary beverages decreased by 82%, change in BMI was 0.07 ± 0.14 kg/m2. Control group: 0.21 ± 0.15 kg/m2. Net difference: -0.14 ± 0.21 kg/m2 (not significant) Among upper baseline-BMI tertile, BMI change in intervention was -0.63 ± 0.23 kg/m2 and in control +0.12 ± 0.26 kg/m2. statistically significant (p= 0.03). Greater effect among subjects who drank more sugar beverages at baseline. No change in physical activity, television viewing or total media time in either group.

**ADVERSE EVENTS:** None.

**ADHERENCE/COMPLIANCE:** Assessed by phone interview, self-report, questionnaire. 83% completed interviews in intervention group.

**ANALYSIS:** Intention-to-treat: Yes

**ADEQUATE RANDOMIZATION:** Yes

**ADEQUATE ALLOCATION CONCEALMENT:** No/ Not possible

**BLINDING OF OUTCOMES ASSESSORS:** Yes (interviewers blinded)

**ATTRITION:** 100% completion rate

**NOTES:** Limitations: relatively small sample size, short intervention period, reliance on self-report, no pubertal status staging (but randomized).

**QUALITY RATING** Good

**STUDY**

**Author:** García-Morales et al

**Year:** 2006

**FUNDING:** Not reported
**RESEARCH OBJECTIVE:** Assess efficacy and safety of sibutramine in obese Mexican adolescents

**METHODS:** Run-in period prior to randomization.

**PARTICIPANTS:** N = 46 (n = 23 sibutramine, n = 23 placebo), ages 14-18 years, BMI > 95th percentile

**INTERVENTION:** 6 months of 10 mg sibutramine daily vs. placebo daily, in addition to individualized recommendations on healthy diet and physical activity.

**OUTCOME ASSESSMENT:** Primary end points: change in body weight, BMI, % BMI
Secondary end points: waist circumference

**RESULTS:**
- Sibutramine group: Net weight loss of 7.3 kg [95% CI, 4.6-9.9], waist circumference loss of 8.0 cm [95% CI, 4.7-11.3], %BMI loss of 9.2% [95% CI, 6.9-11.6].
- Placebo group: Net weight loss of 4.3 kg [95% CI, 1.7-6.9], waist circumference loss of 3.8 cm [95% CI, 0.7-7.0], %BMI loss of 5.2% [95% CI, 2.4-7.9].

Intragroup comparisons, P < 0.05; intergroup comparisons, P > 0.05.

**ADVERSE EVENTS:**
- Sibutramine group: 1 with increased blood pressure, 3 with increased heart rate; Placebo group: 2 with increased blood pressure, 2 with increased heart rate. All subsided within a week and did not lead to withdrawal.
- Mild adverse events: Sibutramine group had 3 patients with headache, dry mouth, headache with nausea and headache with weakness and paleness (p>0.05); Placebo group had 3 patients with 2 cases of headache, 1 case of headache with somnolence and 1 case of headache with dry mouth (p>0.05).

**ADHERENCE/COMPLIANCE:** Pill count
Physical activity successful with completion of 3 days of at least 30 min of exercise.
90-100% compliance rate

**ANALYSIS:** ITT: modified (does not include the data from 5 early drop-out patients).
Last-observation-carried-forward also reported.
Post-randomization exclusions: yes (5 patients who dropped out before 1st month of treatment).

**ADAPRQUATE RANDOMIZATION:** Yes

**ADAPRQUATE ALLOCATION CONCEALMENT:** Yes

**BLINDING OF OUTCOMES ASSESSORS:** Yes

**ATTRITION:** Overall attrition: 6 (13%)
2 drop-outs in sibutramine group, 4 drop-outs in placebo group
<table>
<thead>
<tr>
<th>STUDY</th>
<th>Author: Germann et al\textsuperscript{53}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year:</td>
<td>2006</td>
</tr>
<tr>
<td>FUNDING:</td>
<td>Galter Foundation, Foundation for Health Enhancement, Federick E. and Ida M. Hummel Foundation, Max Goldenberg Foundation</td>
</tr>
<tr>
<td>RESEARCH OBJECTIVE:</td>
<td>To assess the effectiveness of the FitMatters treatment program in morbidly obese, low-income, minority adolescents</td>
</tr>
<tr>
<td>METHODS:</td>
<td>Analysis to determine differences between groups of participants on individual and family measures of behavioral/emotional stability, pretreatment weight control and exercise behaviors, process measures, demographic variables, discriminated between “successful” and “less successful” groups to assess differences. Secondary analysis compared weight gain before and after participating in treatment, by using a comparison group (whose records were available).</td>
</tr>
<tr>
<td>PARTICIPANTS:</td>
<td>N = 150 randomized (76 male, 74 female); follow-up data on 83 participants; age $\geq 8$ years; BMI $\geq 95^{th}$ percentile</td>
</tr>
<tr>
<td>INTERVENTION:</td>
<td>Behavioral intervention, FitMatters program: cognitive-behavioral therapy, nutritional education, medical monitoring and structured exercise training</td>
</tr>
<tr>
<td>Average follow-up:</td>
<td>23 months</td>
</tr>
<tr>
<td>OUTCOME ASSESSMENT:</td>
<td>Primary outcome: BMI z-score</td>
</tr>
<tr>
<td></td>
<td>Process measures: child and parental self-monitoring</td>
</tr>
<tr>
<td></td>
<td>Additional measures: differences between “successful” and “less successful” groups in individual and family measures of behavioral/emotional stability, pretreatment weight control and exercise behaviors, process measures, demographic variables, and compared weight gain before and after participating program with comparison group.</td>
</tr>
<tr>
<td>RESULTS:</td>
<td>Mean BMI z-score change: -0.05, SD = 1.41</td>
</tr>
<tr>
<td></td>
<td>23% achieved clinically meaningful weight change, defined as -0.70 z-scores or better.</td>
</tr>
<tr>
<td>ADVERSE EVENTS:</td>
<td>None reported</td>
</tr>
<tr>
<td>ADHERENCE/COMPLIANCE:</td>
<td>83 (55.3%) participated in follow-up</td>
</tr>
<tr>
<td></td>
<td>Compliance in program unclear</td>
</tr>
<tr>
<td>ANALYSIS:</td>
<td>ANOVA</td>
</tr>
<tr>
<td>ADEQUATE RANDOMIZATION:</td>
<td>Not applicable</td>
</tr>
<tr>
<td>ADEQUATE</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
ALLOCATION CONCEALMENT: | Not possible
---|---
BLINDING OF OUTCOMES ASSESSORS: | Not reported
ATTRITION: | 67 (44.7%)
NOTES: | Looked at differences that might correlate with success
QUALITY RATING | Poor

| STUDY | Author: Johnston et al
Year: 2007 |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>FUNDING:</td>
<td>US Department of Agriculture grant</td>
</tr>
<tr>
<td>RESEARCH OBJECTIVE:</td>
<td>Evaluate an intensive healthy lifestyle intervention for weight loss in overweight Mexican-American children compared to a self-help program.</td>
</tr>
<tr>
<td>METHODS:</td>
<td>Follow-up at 3 and 6 months</td>
</tr>
<tr>
<td>PARTICIPANTS:</td>
<td>N = 60 (33 boys); ages 10-14; ≥ 85th percentile in BMI for age and sex; randomized 2:1 (40 treatment, 20 control)</td>
</tr>
<tr>
<td>INTERVENTION:</td>
<td>12 weeks of instructor-led intervention with daily sessions during school followed by 12 weeks of biweekly sessions vs. 12 week self-help parent-guided manual (Trim Kids).</td>
</tr>
<tr>
<td>OUTCOME ASSESSMENT:</td>
<td>Primary: BMI, %BMI, BMI z-score Secondary: cholesterol, blood pressure, insulin</td>
</tr>
</tbody>
</table>
| RESULTS: | zBMI change: F = 12.74, P < 0.001
*Intervention (II):* Weight: – 1.75 ± 10.34 kg, BMI: – 1.16 ± 4.17 kg/m², %BMI: – 2.81 ± 4.42
*Control (I):* Weight: + 1.31 ± 1.53 kg, BMI: + 0.29 ± 0.51 kg/m², %BMI: + 0.02 ± 1.69 |
| ADVERSE EVENTS: | None reported |
| ADHERENCE/COMPLIANCE: | Biweekly quizzes to test if children were learning the material; point system/rewards for participation |
| ANALYSIS: | ITT: Yes Post-randomization exclusions? No |
| ADEQUATE RANDOMIZATION: | Yes |
| ADEQUATE ALLOCATION CONCEALMENT: | Not possible |
| BLINDING OF OUTCOMES ASSESSORS: | Not reported |
| ATTRITION: | 3 (95% completion rate) |
**NOTES:**
Minimal exclusion criteria among overweight Mexican-American children.
Included cultural considerations in treatment

**QUALITY RATING**
Fair

| STUDY | **Author:** Resnicow et al<sup>76</sup>  
**Year:** 2000 |
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>FUNDING:</strong></td>
<td>CDC</td>
</tr>
<tr>
<td><strong>RESEARCH OBJECTIVE:</strong></td>
<td>Evaluate a behavioral intervention in overweight, low-income, African-American adolescent females</td>
</tr>
<tr>
<td><strong>METHODS:</strong></td>
<td>Recruited from public housing development; N = 57; ages 11-17; BMI ≥ 85&lt;sup&gt;th&lt;/sup&gt; percentile for age and sex;</td>
</tr>
<tr>
<td><strong>INTERVENTION:</strong></td>
<td>Behavioral intervention based on social cognitive theory that focused on increasing fruit and vegetable uptake, decreasing fat intake, decreasing fast food intake, decreasing television viewing and increasing physical activity.</td>
</tr>
</tbody>
</table>
| **OUTCOME ASSESSMENT:** | Physiologic measures: BMI, % body fat, DXA, cholesterol, blood pressure and aerobic capacity  
Physical activity and sedentary behaviors reported based on 1 week recall  
Psychosocial measures: self-esteem, preoccupation with weight and food, social support, self-efficacy, health knowledge and perceived weight  
Compared high (> 50% of sessions) and low attendees (groups differed in baseline cholesterol and blood pressure) |
| **RESULTS:** | No significant difference between high and low attendees for any physical measure (slight trend favoring high attendees); high attendees had significantly greater nutrition knowledge scores, reported significantly more low-fat intake, were more likely to perceive positive dietary changes, reported more social support.  
Based on raw change values, both groups showed an increase in body weight and BMI. |
| **ADVERSE EVENTS:** | None reported. |
| **ADHERENCE/COMPLIANCE:** | On average, girls attended 43% of sessions  
Point system/rewards to encourage participation |
| **ANALYSIS:** | Analysis of variance |
| **ADEQUATE RANDOMIZATION:** | Not applicable |
| **ADEQUATE ALLOCATION:** | Not applicable |
### Study

**Author:** Savoye et al. 2007  
**Year:** 2007

**Research Objective:** Compare effects of weight management intervention (Bright Bodies) on body composition and metabolic parameters in overweight children over control.

**Methods:**  
**Participants:** N = 209; ages 8 – 16; BMI > 95th percentile  
**Intervention:** Control group had traditional clinical weight management counseling every 6 months vs. intervention group had intensive family-based program (biweekly the first 6 months, bimonthly after) including exercise, nutrition and behavioral modification for participants and caregivers. Weight management group with structured meal plan approach was discontinued due to high drop out rate (83% drop-out rate at 6 months).

**Outcome Assessment:** Weight, BMI, body fat, insulin resistance at 6 and 12 months.

**Results:** Treatment effect:  
- Weight: 7.6 kg at 6 months, 7.4 kg at 12 months (p < 0.001)  
- BMI: 3.1 kg/m² at 6 mths, 3.3 kg/m² at 12 mths (p < 0.001)  
- % body fat: 5.2 at 6 mths, 6.0 at 12 mths (p < 0.001)  
- Change in BMI (kg/m²): intervention -2.1 (95% CI -2.6 to -1.5) at 6 mths, -1.7 (95% CI -2.3 to -1.1) at 12 mths vs. control +1.1 (95% CI 0.4 to 1.8) at 6 mths, +1.6 (95% CI 0.8 to 2.3) at 12 mths  
- Significant difference in fasting insulin (treatment -1.51 vs. control +0.33 at 6 mths, treatment -1.52 vs. control +0.90 at 12 mths).

**Adverse Events:** None reported

**Adherence/Compliance:** Heart rate monitor worn during exercise to ensure adequate intensity  
Attendance not reported

**Analysis:** ITT: yes
<table>
<thead>
<tr>
<th>Post-randomization exclusions? Study arm discontinued</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADEQUATE RANDOMIZATION:</td>
<td>Not possible</td>
</tr>
<tr>
<td>ADEQUATE ALLOCATION CONCEALMENT:</td>
<td>Not reported</td>
</tr>
<tr>
<td>BLINDING OF OUTCOMES ASSESSORS:</td>
<td>Limited to English-speaking</td>
</tr>
<tr>
<td>ATTRITION:</td>
<td>No statistical significance in drop-out rates among ethnic groups (minority participants with somewhat greater retention than white participants)</td>
</tr>
<tr>
<td>NOTES:</td>
<td>QUALITY RATING: Poor</td>
</tr>
</tbody>
</table>

**STUDY**

**Author:** Srinivasan et al

**Year:** 2006

**FUNDING:** National Health Medical Research Scholarship, Diabetes Australia Research Trust grant

**RESEARCH OBJECTIVE:** Examine the effects of metformin on body composition and insulin sensitivity in obese pediatric patients

**METHODS:** 2 weeks wash-out, cross-over design

**PARTICIPANTS:** N = 28 (13 males); ages 9-18 years; 64% from other racial/ethnic background in Australia, included more Pacific Islanders, Indians; clinical suspicion of insulin resistance; 13 participants to metformin first, then placebo; 15 participants to placebo then metformin.

**INTERVENTION:** Metformin 1 g twice daily vs. placebo for 6 months (cross-over design)

**OUTCOME ASSESSMENT:** Weight, height, BMI, BMI z-score, waist circumference, glucose tolerance test, blood pressure, DXA imaging, abdominal MRI

**RESULTS:** Metformin treatment effect: Weight -4.35 kg (p = 0.02); Weight z-score -0.09 kg (p=0.009); BMI -1.26 kg/m² (p = 0.002); BMI z-score -0.12 kg/m² (p = 0.005)

Improvements in fasting serum glucose and insulin, but not insulin sensitivity.

**ADVERSE** Nausea (2 participants, age 9, unable to tolerate 1 g metformin)
## EVENTS:
but tolerated 750mg twice daily after slow increments
No difference in LFTs, serum creatinine or lactate levels.

## ADHERENCE/COMPLIANCE:
Pill count every 3 months
Metformin median adherence 78% (15-99%); placebo median adherence 78% (35-98%)
8 patients took less than 75% of metformin

## ANALYSIS:
ITT: T-tests (cross-over study)
Post-randomization exclusions? No

## ADEQUATE RANDOMIZATION:
Yes

## ADEQUATE ALLOCATION CONCEALMENT:
Yes

## BLINDING OF OUTCOMES ASSESSORS:
Yes

## ATTRITION:
Overall: 4 (1 in group A, 3 in group B)
Nonadherence to therapy or social circumstances

## NOTES:
2 without full set of insulin sensitivity data because of IV access, but does not affect key question of SR
Adjusted for puberty and poor adherence to therapy on insulin sensitivity

## QUALITY RATING
Good

## STUDY
Author: Williamson et al
Year: 2006

## FUNDING:
NIH

## RESEARCH OBJECTIVE:
Assess efficacy of internet-based lifestyle intervention program in obese African-American girls

## METHODS:

### PARTICIPANTS:
N = 57; African-American females; ages 11 – 15; overweight or obese with BMI > 85th percentile for age and sex; at least one obese (BMI > 30) biological parent and one overweight (BMI > 27) parent willing to participate in study

### INTERVENTION:
Interactive behavioral internet program (treatment) vs. internet health education program (control) over 24 months.
Treatment arm included nutrition education and internet counseling behavior modification program focused on eating habits and physical activity, in addition to 4 face-to-face counseling sessions during the first 12 weeks. Control arm included education on healthy nutrition and exercise, but no counseling or recommended behavioral changes (passive).

### OUTCOME
Measured at 6, 12, 28 and 24 months
<table>
<thead>
<tr>
<th><strong>ASSESSMENT:</strong></th>
<th>BMI, %BMI, DXA, weight loss behavior scale, web site use (log on required),</th>
</tr>
</thead>
</table>
| **RESULTS:**    | Treatment: BMI +0.73 ± 0.66, %BMI – 0.004 ± 0.003  
Control: BMI +1.2 ± 0.65, %BMI – 0.001 ± 0.003  
Significant difference in % body fat seen in first 6 months, but did not significantly differ at 2 years. |
| **ADVERSE EVENTS:** | None reported |
| **ADHERENCE/COMPLIANCE:** | 100% attendance for completers at face-to-face counseling sessions  
Self-report for exercise, eating habits |
| **ANALYSIS:** | ITT: Yes  
Post-randomization exclusions? No |
| **ADEQUATE RANDOMIZATION:** | Not reported |
| **ADEQUATE ALLOCATION CONCEALMENT:** | Not possible |
| **BLINING OF OUTCOMES ASSESSORS:** | No |
| **ATTRITION:** | 17 (7 control, 10 treatment)  
70% completion rate (adolescent-parent dyads) |
| **NOTES:** | Limiting factor for external validity: family willing to pay $300 towards purchase of computer (worth $1000); home with electricity and at least one functional telephone line (program included free internet access) |
| **QUALITY RATING** | Poor |

*Adolescent participant results only reported. Did not include parental results.*