

# OBESITY CLINICAL TRIALS IN YOUTH: CONCEPTS AND CHALLENGES

Donna B. Moore, MD

## INTRODUCTION

The impact of obesity related morbidity is receiving increased attention in the pediatric population with the emergence of type 2 diabetes mellitus, as well as an increase in the prevalence of hypertension.<sup>1</sup> The Centers for Disease Control and Prevention released preliminary data from the 1999 National Health and Nutrition Examination Survey, indicating a rise in the prevalence of overweight children (body mass index >95th percentile), from 11% to 13–14%.<sup>2</sup> Despite recognizing this as a major health issue, little success has been made to arrest the trend. Research in the area of obesity is broad and multi-factorial, encompassing genetic, biological, social, and behavioral components in an attempt to delineate the determinants for the development of obesity. Several clinical trials on obesity in children examine interventions for either obesity prevention or treatment. This paper will summarize the essential components of the studies pertaining to youth and obesity prevention and treatment, as well as give direction to future areas of research.

by primary prevention, which hinders the onset of obesity in normal weight subjects, or by secondary prevention which prevents obese subjects from becoming more obese. In contrast, weight loss treatment studies emphasize the ability to show significant results in inducing weight loss among obese patients. The study population chosen will generally reflect the primary study goal. Normal weight subjects who would not need to lose weight, logically would be targeted for obesity prevention studies. Overweight or obese subjects, however, may be appropriate to recruit for further weight gain prevention or weight loss intervention studies.

Basic differences also exist as to how these 2 types of intervention studies are designed.<sup>3</sup> The duration of a prevention study extends over several months, usually greater than one year, allowing a reasonable period of time for followup. Treatment studies, however, are generally completed in less than 12 months. Study sample sizes in prevention studies tend to be moderate-to-large in number and interventions are applied to large groups at a time. In contrast, the number of participants in treatment studies are small-to-moderate with interventions targeted for small groups at a time.

## Intervention Modalities

Despite whether the emphasis of the study is prevention or treatment, there are some common elements that can be observed in respect to intervention modalities. Essentially, interventions can be grouped into 3 types of categories: dietary, physical activity, or behavior modification.

The use of diet as a sole intervention is based on the premise that if energy consumption is less than or equivalent to energy expenditure, the net result will

## CHARACTERISTICS OF CLINICAL TRIALS

### Study Emphasis

One of the fundamental elements that is crucial to understanding any type of study is to recognize the emphasis and focus. Prevention and treatment are 2 perspectives from which obesity studies in children are addressed, the emphasis of each having quite different characteristics. The goal of weight gain prevention studies is to demonstrate the prevention of abnormal weight gain development.<sup>3</sup> These goals can be achieved

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From the Department of Pediatrics, Medical College of Georgia, Augusta, Georgia.

Address correspondence and reprint requests to Donna B. Moore, MD; Assistant Professor; Department of Pediatrics; Medical College of Georgia; 1120 Fifteenth Street, BG-2120; Augusta, GA 30912-3770; 706-721-2456; 706-721-3295 (fax); dmoore@mail.mcg.edu

produce weight loss, or at minimum, weight maintenance.<sup>3</sup> There are several types of diets found in the literature, some of which have varying degrees of caloric restriction.<sup>4-7</sup> Other types of diets may restrict specific macro nutrients such as carbohydrates, as in the protein-sparing modified fast.<sup>8</sup> Traffic light diets are commonly used in school-aged children and provide a guideline for food choice selection. The traffic light diet groups foods into categories: green foods may be consumed in unlimited quantities; yellow foods have average nutritional value for the foods within their food group; and red foods provide less nutrient density per calorie because of high fat or simple carbohydrate content.<sup>9</sup> Dietary modifications are intended to be either short term or long term, the latter of which would promote continued lifestyle changes.

The role of exercise is to increase energy expenditure to induce negative energy balance.<sup>3</sup> The concept of exercise is broad and applies to varying states of activity. The spectrum of goals ranges from decreasing sedentary activities to encouraging increased levels of physical activity, thus the intervention may not necessarily promote vigorous exercise but instead discourage more sedentary behaviors.

Behavior modifications can be very complex. There are a multitude of approaches that can be used for interventions involving individuals, families, schools, and communities. Within these operational groups, specific methods such as self-monitoring, contracting, positive reinforcement, and modeling may be employed.

### Measurement Outcomes

Another aspect of any clinical trial is the evaluation of the effectiveness of an intervention, creating a need to establish outcome measures. In obesity studies specifically, several different outcome measures may be identified; however, not all may be significantly affected by intervention efforts. The predominant

outcome measure for both prevention and treatment studies is the body mass index (BMI). Variations of BMI include body weight, percent body fat, percent overweight, and skinfold measurements.<sup>9-12</sup> Intervention effects can also be measured by cardiorespiratory fitness, blood pressure, and biochemical markers, such as insulin and serum lipids.<sup>10-12</sup> Additionally, outcomes may be measured by knowledge-based information regarding nutrition and physical activity, or actual changes in behaviors, physical activity, or dietary habits.<sup>11</sup>

## OBESITY PREVENTION TRIALS

For youth, there are very few studies conducted that emphasize weight gain prevention as a primary outcome; however, many related studies pertaining to prevention of cardiovascular disease risk factors are found in the literature, but are beyond the scope of this discussion. Interestingly, the majority of those studies are school-based and not carried out in strict clinical settings. One of the earliest clinical research studies conducted by Pisacano et al<sup>13</sup> involved a diet-based intervention for a multiethnic, mixed gender population of 130 infants in the first year of life in Long Branch, New York. The control group ate a conventional diet for that era, while the intervention group was placed on The Prudent Diet regimen, which was designed to reduce the intake of saturated fat, sugar, and salt. The conclusion of the study, with subjects at 3 years of age, was that the prevalence of overweight was significantly lower in the intervention group than in the control group.

Robinson<sup>10</sup> demonstrated that significant differences in BMI, waist, triceps, and waist-to-hip (WHR) could be observed between 2 schools, one of which received a classroom curriculum-based intervention while the other did not. The intervention was targeted to decrease time spent watching television

or videotapes or playing video games. Additionally, significant differences were also appreciated in the amount of television viewed and the number of meals eaten in front of the television. No significant differences, however, were noted between the 2 groups in the amount of high fat foods consumed, amount of moderate-to-vigorous exercise and level of fitness. Eighty percent and 70% of the intervention and control group, respectively, were comprised of White participants, with more than 80% being female in each group. The conclusion from this study was that decreasing sedentary behavior would result in less adiposity.

Story<sup>14</sup> published findings from a 2-year multi-modality primary prevention study among 8- to 10-year-old children in 2 rural Nebraska schools. The interventions included classroom nutrition education, enhanced aerobic-type physical education, and a modified school lunch diet, which was lower in fat than the usual lunch. Although obesity was not significantly affected in the intervention group compared to the control group, there were positive intervention effects for lowering fat in school lunches and increases in student nutrition education knowledge.

Planet health,<sup>15</sup> also a 2-year, school-based prevention study of 1,295 ethnically diverse 6th to 8th grade children, compared 5 control schools to 5 intervention schools in Boston, Mass. The focus of this intervention targeted 4 behavioral changes: reducing television viewing, increasing moderate and vigorous physical activity, decreasing consumption of high fat foods and increasing consumption of fruits and vegetables through an interdisciplinary curriculum approach. The results demonstrated the success of intervention effects of decreasing the prevalence of obesity, and also decreasing the likelihood of girls, particularly Black, developing obesity, but this same effect was not seen for boys. Also noted was a reduction in television viewing among the intervention group compared to the control group.

Presently there are ongoing prevention trials worthy of mention, one being the Pathways Study<sup>16</sup> for the prevention of obesity in American Indian school children, another is the Stanford Obesity Prevention for Pre-Adolescent (OPPrA) trial.<sup>3</sup> The Pathways Study<sup>16</sup> is designed to be culturally sensitive for 3rd grade children and consists of programming for health promotion, physical education, school meals, and family involvement. The OPPrA trial<sup>3</sup> is another multi-component intervention comprised of classroom curriculum, physical education, and school lunch intervention. It is difficult to draw conclusions regarding the efficacy of these interventions, being few in number with varying degrees of significant results: however, it seems reasonable to believe, that particularly the population approach to prevention, would yield favorable results once effective strategies are identified.

### OBESITY TREATMENT TRIALS

In contrast to prevention trials, more research has been conducted in the area of obesity treatment in youth. Epstein et al<sup>9</sup> summarizes several clinical works that have been published, highlighting the salient features of the interventions and outcomes of each study. There were 32 studies with youth whose ages ranged from 2–18 years of age, predominantly mixed gender and White populations. The majority of the studies included diet and the remaining included nutrition information. A diet-only intervention was described in only one study, which was designed to evaluate the efficacy of supplemental fiber. All but 2 studies involved either exercise or exercise information. Behavioral modification was integral to most of the studies reviewed.

There were a few main conclusions that could be made in regards to diet as an intervention for the treatment of

obesity in youth. The first being that diet was rarely implemented as a sole intervention, primarily based on previous studies that demonstrated better results in combination with exercise.<sup>17</sup> In pre-adolescent children, the use of traffic light diets were shown to have significant results not only in decreasing obesity in the short term, but also in changing eating patterns and maintaining long term effects when combined with behavior modification and exercise.<sup>9,18</sup> More restrictive diets, such as protein-sparing modified fasts, were used for the treatment of severe obesity, primarily in adolescents. Short term results yielded significant weight loss, however at 15-month followup, there was no significant difference in the decrease in percent overweight compared to a less restrictive hypocaloric diet.<sup>8</sup> Not included in Epstein's review, is a study conducted by Spieth<sup>19</sup> involving a cohort of 107 obese multiethnic, mixed gender children, 6 to 14 years of age. The cohort was assigned into 2 groups, one of which received a low-fat diet, the other a low-glycemic index diet. Eighty four percent of the low-glycemic index group and 53% of the low-fat group were comprised of White subjects. The low-glycemic index group had a significantly greater decrease in BMI and body weight.

Exercise without diet intervention has not significantly impacted changes in weight.<sup>3</sup> Merely increasing caloric expenditure without modifying caloric consumption generally does not produce desired weight loss results. Several different physical activity interventions have been implemented of varying intensity, frequency, and duration. Aerobic, lifestyle, and calisthenic exercise are examples of activities that have been carried out in either supervised or home settings, with once a week to daily participation, between 20 to 60 minutes each session. Of the few studies that compared lifestyle to aerobic exercise, percent overweight changes were significantly more favorable in those who par-

ticipated in increasing energy expenditure in regular daily (life style) activities rather than in programmed aerobic activity.<sup>9</sup>

Similarly varied are the approaches to behavior modification. Many types of interventions have been described in the literature including: individual, parent-child pairs or family behavior therapy; gradual or rapid behavioral treatment; reinforcement of alternative sets of behaviors; and problem solving training.<sup>9</sup> Some studies have shown that parental involvement in behavior therapy adds to treatment effects while others have not.<sup>7,8,18</sup> Longer durations of behavior treatment seem to be more effective than "crash" courses in terms of achieving significant weight change.<sup>9</sup> Reinforcement of decreasing sedentary behaviors such as television viewing, demonstrated greater weight loss than reinforcing an increase in activity.<sup>10–12</sup> The summation of these studies would suggest that behavior therapy enhances outcome effects favorably, although variably, depending on the specific intervention and should be used as an adjunct in the treatment of obesity in youth.

School-based treatment studies summarized by Story,<sup>14</sup> essentially paralleled in results, and found significantly greater decreases in percent overweight among intervention groups compared to controls. All studies except one included at least 2 intervention modalities: nutrition education and physical activity. Other studies included an additional component of behavior modification with or without parental involvement. Generally, intervention effects were better demonstrated among younger children than adolescents and were greater among heavier children. The impact of parental involvement yielded mixed results.

### TRIAL CHALLENGES

As with almost any type of study, the issue of compliance can contribute to

the degree of success demonstrated. Few studies indicated how adherence to protocols was monitored, which may have influenced the outcome of the studies. Depending on the recruitment methodology, some participants may have been less motivated than others to participate and potentially could have underestimated the effectiveness of the intervention. It is also difficult to determine which interventions were superior, since there were many variables within, as well as between, studies, making direct comparisons challenging. For example, was it the form or the frequency of physical activity that yielded the best results and how might interactions with varying dietary modifications have influenced those results? It still seems to be unclear as to whether interventions should be different between genders or age groups. Also uncertain is whether these same studies, when applied to specific populations, such as Blacks and other non-White ethnic groups, would yield at least the same favorable results. Future studies in ethnically diverse youth populations will need to specifically identify which dietary modifications, behavioral strategies, and forms of physical activity, in the context of age and gender, will be effective in the prevention and treatment of pediatric obesity.

#### REFERENCES

1. Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics*. 1998;101:518–525.
2. *Prevalence of Overweight Among Children and Adolescents: United States, 1999, 2001*. Hyattsville, Md: National Center for Health Statistics; 2001.
3. Fulton JE, McGuiere MT, Caspersen CJ, Dietz WH. Interventions for weight loss and weight gain prevention among youth. *Sports Med*. 2001;31:153–165.
4. Becque MD, Katch VL, Rocchini AP, Marks CR, Moorehead C. Coronary risk incidence of obese adolescents: reduction by exercise plus diet interventions. *Pediatrics*. 1988;81:605–612.
5. Rocchini AP, Katch V, Anderson J, et al. Blood pressure in obese adolescents: effect of weight loss. *Pediatrics*. 1988;82:16–23.
6. Flodmark CE, Ohlsson T, Ryden O, Sveger T. Prevention of progression to severe obesity in a group of obese school children treated with family therapy. *Pediatrics*. 1993;91:880–884.
7. Wadden TA, Stunkard AJ, Rich L, Rubin CJ, Sweidel G, McKinney S. Obesity in Black adolescent girls: a controlled clinical trial of treatment by diet, behavior modification, and parental support. *Pediatrics*. 1990;85:345–352.
8. Figueroa-Colon R, von Almen TK, Franklin FA, Schuftan C, Suskind RM. Comparison of two hypocaloric diets in obese children. *Am J Dis Child*. 1993;147:160–166.
9. Epstein LH, Myers MD, Raynor HA, Saelens BE. Treatment of pediatric obesity. *Pediatrics*. 1998;101:S554–S570.
10. Robinson TN. Reducing children's television viewing to prevent obesity: a randomized controlled trial. *JAMA*. 1999;282:1561–1567.
11. Epstein LH, Paluch RA, Gordy CC, Dorn J. Decreasing sedentary behaviors in treating pediatric obesity. *Arch Pediatr Adolesc Med*. 2000;154:220–226.
12. Epstein LH, Goldfield GS. Physical activity in the treatment of childhood overweight and obesity: current evidence and research issues. *Med Sci Sports Exerc*. 1999;31:S553–S559.
13. Pisacano JC, Lichter H, Ritter J, Siegal AP. An attempt at prevention of obesity in infancy. *Pediatrics*. 1978;61:360–364.
14. Story M. School-based approaches for preventing and treating obesity. *Int J Obes Relat Metab Disord*. 1999;23:S43–S51.
15. Gortmaker SL, Peterson K, Wiecha J, et al. Reducing obesity via a school-based interdisciplinary intervention among youth: Planet Health. *Arch Pediatr Adolesc Med*. 1999;153:409–418.
16. Davis CE, Hunsberger S, Murray DM, et al. Design and statistical analysis for the Pathways study. *Am J Clin Nutr*. 1999;69:760S–763S.
17. Epstein LH, Wing RR, Penner BC, Kress MJ. Effect of diet and controlled exercise on weight loss in obese children. *J Pediatr*. 1985;107:358–361.
18. Edmunds L, Waters E, Elliott EJ. Evidence based pediatrics: evidence based management of childhood obesity. *BMJ*. 2001;323:916–919.
19. Spieth LE, Harnish JD, Lenders CM, et al. A low-glycemic index diet in the treatment of pediatric obesity. *Arch Pediatr Adolesc Med*. 2000;154:947–951.

#### AUTHOR CONTRIBUTIONS

*Design and concept of study:* Moore

*Acquisition of data:* Moore

*Data analysis and interpretation:* Moore

*Manuscript draft:* Moore