# Exercise for Prevention of Obesity and Diabetes in Children and Adolescents

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## **KEYWORDS**

- Obesity prevention Diabetes prevention Obesity Diabetes
- Childhood obesity prevention Type 2 diabetes prevention
- Childhood diabetes prevention

In preindustrial times, our ability to store fat undoubtedly led ironically to the "survival of the fittest." In the Paleolithic and Mesolithic eras, conditions of feast or famine required the ability to store fat in times of need. Hunting and foraging resulted in avolatile food supply and required constant human movement. Even as humans transitioned to an agricultural age in the Neolithic period, these preindustrial societies required large energy expenditures in animal husbandry and plant cultivation in the absence of mechanization.

In today's world of labor stratification, declining physical exercise, and easy access to energy-dense foods, or otherwise what is often termed an "obesogenic" environment, the model of what was once advantageous to survival is no longer the case. Heart disease is the leading cause of mortality in the United States, with cerebrovascular disease and diabetes well within the top 10 causes of death.<sup>1</sup> All 3 of these have been linked to obesity and the metabolic syndrome.

Obesity often predisposes patients to type 2 diabetes, hypertension, and dyslipidemia or the metabolic syndrome largely through the production of increased free fatty acids and adipokines by the increased amounts of adipose tissue. With increased lipolysis in obesity, there is increased free fatty acid production, which interferes with insulin receptor signaling and leads to decreased glucose transport, often referred to as lipotoxicity. Increased fatty acids ultimately result in activating protein kinase C (through increased fatty Acyl-CoA and diacylglycerols), and, in turn, protein kinase C serine phosphorylates the insulin receptor, interfering with insulin signal

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transduction. Increased free fatty acids also impair phosphoinositide (PI)-3 kinase activation in response to insulin, which results in downstream decreased activity of glucose transporter-4 (GLUT4), an important insulin-sensitive glucose transporter in muscle and fat. In an obese state, some adipokines, proteins such as tumor necrosis factor alpha (TNF- $\alpha$ ), or cytokines such as interleukin-6 (IL-6) are elevated, whereas adiponectin, an insulin-sensitizing adipokine, is low. Adipokines inhibit insulin action and contribute to proinflammatory effects, insulin resistance, and endothelial dysfunction. This eventually results in an increased risk for myocardial infarction and stroke.

## **OBESITY PREVALENCE**

The fact that obesity is the largest epidemic of our times is confirmed by the most recent NHANES data for 2005 to 2006 indicating that the prevalence of obesity among adults is 34%.<sup>2</sup> This is in contrast to just 20 years ago, when age-adjusted obesity rates in NHANES III 1988 to 1994 were 23%. A visual representation of the US distribution of obesity can be seen in **Fig. 1**, with only 1 state (Colorado) currently with a prevalence of adult obesity less than 20% and most of the country with a prevalence of obesity greater than 25%.

Adult obesity is also reflected in rates of childhood overweight and obesity. NHANES data for the combined years of 2003 to 2006 indicate that 16.3% of children and adolescents aged 2 to 19 years are obese, defined as at or above the 95th percentile of the 2000 body mass index (BMI)-for age growth charts.<sup>3</sup> This is compared with about 5% in NHANES III data from 1988 to 1994. This is even more striking when considering the number of children at risk for obesity currently. NHANES survey data from 2003 to 2006 find that 32% of the children in the United States are overweight, defined as at or above the 85th percentile of the 2000 BMI-for age growth charts. **Fig. 2** illustrates the trend in overweight rates for selected years from 1976 to 2004.

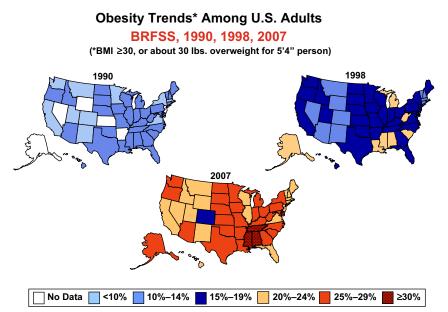


Fig. 1. Obesity trends. (*Adapted from* Centers for Disease Control. U.S. Obesity Trends 1985–2007. Available at: http://www.cdc.gov/nccdphp/dnpa/obesity/trend/maps/#PDF.)

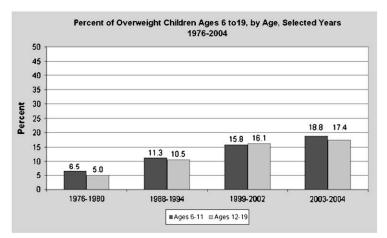


Fig. 2. Overweight trends for children. (*Courtesy of* Child Trends Data Bank, Washington, DC; with permission.)

The rise in obesity has not been confined to the United States. According to a pooled analysis of worldwide data in 2005, 23.2% of the world's population is overweight, with a BMI of 25 kg/m<sup>2</sup> or greater. About 8% of the world's population is obese, with a BMI at or greater than 30 kg/m<sup>2</sup>.<sup>4</sup> Although the prevalence of overweight and obesity was higher in developed countries than that in developing countries (35.2% vs 19.6% and 20.3% vs 6%, respectively) the larger population in developing countries results in an overall larger global population being affected. This is also supported by World Health Organization (WHO) data (refer to **Fig. 3**). If current trends continue, the WHO predicts that there will be 2.3 billion overweight adults in the world by 2015, and more than 700 million of them will be obese.

In terms of worldwide childhood obesity, defining overweight as a weight-for-height greater than 2 standard deviations above the National Center for Health Statistics/ WHO international reference median, one study found that the global prevalence of overweight was 3.3% in children.<sup>5</sup> Although childhood malnourishment is still a critical concern in many countries, the number of overweight children is growing, with the highest overweight prevalence rates in the Americas, Europe, and the Middle East, according to data from the International Obesity Task Force (**Fig. 4**).

### **OBESITY PREVENTION IN ADULTS**

Preventing obesity in adults has largely been studied in selected populations or in the context of preventing diabetes. A small randomized, controlled trial (n = 40) known as the Health Hunters pilot study focused on young women with at least 1 obese parent.<sup>6</sup> The study found that an intervention dedicated to improving physical activity and diet resulted in weight stability compared with the weight gain in the control group after 1 year. Another randomized controlled trial studied older women.<sup>7</sup> This trial was larger (n = 173) and involved overweight, obese, postmenopausal women who were randomized to either 45 minutes of moderate-intensity physical exercise 5 d/wk or the control group. The exercise group had a significant decrease in body weight (-1.4 kg), total body fat (-1.0%) as studied by dual-energy x-ray absorptiometry (DXA), intra-abdominal fat (-8.6 g/cm<sup>2</sup>), and subcutaneous abdominal fat (-28.8 g/cm<sup>2</sup>) as studied by computed tomography at 1 year. These studies were small and

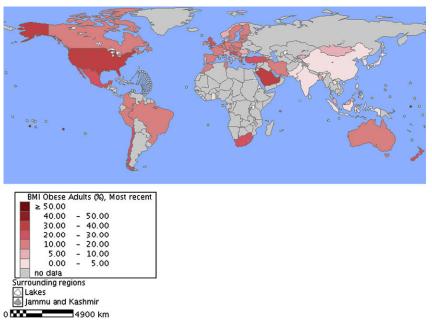
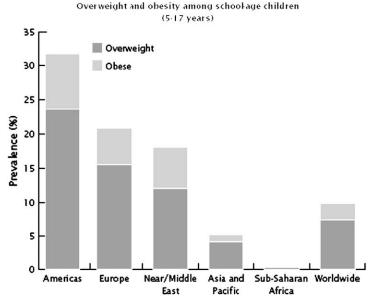


Fig. 3. Global Prevalence of obesity, from the WHO 2005. Obesity is defined as BMI equal to or greater than 30%. (*Courtesy of* the World Health Organization. Global database on body mass index. Available at http://www.who.int/bmi/index.jsp.)



**Fig. 4.** Worldwide childhood obesity prevalence. (*From* International Diabetes Foundation. Diabetes atlas. 2nd edition. Brussels: International Diabetes Foundation; 2003; with permission. Available at: www.eatlas.idf.org.)

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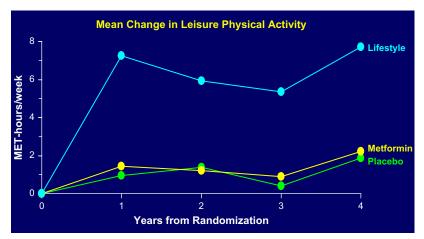
lacked long-term follow-up data but suggested that interventions involving diet and exercise could be useful in preventing obesity in women.

#### DIABETES PREVENTION IN ADULTS

The Finnish Diabetes Prevention study was designed to determine if type 2 diabetes can be prevented by behavioral lifestyle modifications, emphasizing diet and exercise.<sup>8</sup> The study enrolled 523 middle-aged patients with a BMI at or greater than 25 kg/m<sup>2</sup>, with impaired glucose tolerance as determined by an oral glucose tolerance test (OGTT). It used the older 1985 WHO definition of diabetes as a fasting blood glucose greater than 140 mg/dL. Subjects were either randomized to a control group, with some general information on diet and exercise, or the intervention group, who received detailed individualized diet and exercise information. The intervention group also received individual nutritionist sessions and weight training sessions. The goals of the lifestyle intervention included 5% body weight loss, 30% decrease in total fat intake with a 10% decrease in saturated fats, increased fiber, and moderate exercise for at least 30 minutes daily. After 2 years of enrollment in the study, the intervention group had a mean 3.5-kg loss in weight compared with a 0.8-kg loss in the control group. Only 27 patients were diagnosed with diabetes in the intervention group compared with 59 in the control group at the end of the study. The risk of diabetes was thus reduced in the intervention group by 58% (P<.001). In fact, none of the patients in either the intervention group (49) or the control group (15) who reached 4 out of the 5 goals developed diabetes. This suggests that individualized lifestyle interventions can decrease the risk of diabetes by 58% and almost 100% in those patients meeting the goals of this intervention. After 3 years of follow-up, the intervention group had a 36% decrease in the risk of diabetes.

The Finnish Diabetes Prevention Study significantly reduced cardiometabolic risk through an effective intervention with relatively modest goals. The long-term data from the Finnish Diabetes Study indicated that a difference between the groups remained 7 years after the end of the study, with incidence rates for the intervention group at  $4 \cdot 3$  (95% confidence interval [CI],  $3 \cdot 4 - 5 \cdot 4$ ) and for the control at  $7 \cdot 4$  ( $6 \cdot 1 - 8 \cdot 9$ ) per 100 person years.<sup>9</sup> The cumulative incidence of diabetes at year 6 was 23% in the intervention group and 38% in the control group, with an absolute risk reduction of 15% ( $7 \cdot 2 - 23 \cdot 2$ ). The relative risk reduction was 43%, which was less than the 58% seen during the original study. As expected, several subjects went on to develop diabetes over the follow-up period of 7 years. The results of the original Finnish Diabetes Prevention Study were convincing enough to lead to a national diabetes prevention program that has been implemented in Finland, which initially identifies high-risk individuals with a simple, validated risk-score questionnaire.<sup>10</sup>

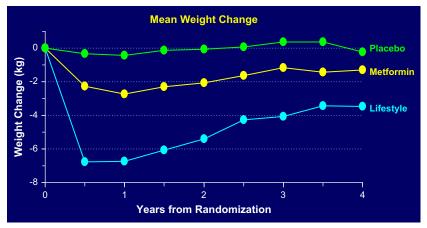
The DPP was another large randomized, controlled trial in adults, aimed at identifying effective methods for the prevention of diabetes.<sup>11</sup> The study had 3234 overweight or obese subjects, with impaired fasting glucose and impaired glucose tolerance, who were randomized to standard lifestyle changes, standard lifestyle changes and metformin, or intensive lifestyle changes. Standard lifestyle changes involved provision of written information and 1 20- to 30-minute individual session annually. By comparison, the intensive lifestyle arm involved 16 individualized sessions, with goals to decrease weight by 7% through a low-fat diet and 150 minutes of moderately intense physical activity per week (mostly walking). About 74% of the subjects in the intensive arm were able to meet the goals for physical activity at 24 weeks, and 54%, at the last visit. **Fig. 5** offers a comparison in MET (metabolic equivalent of task) hours per week between the lifestyle, metformin, and placebo groups in



**Fig. 5.** Change in physical activity in DPP trial. (*Courtesy of* the Diabetes Prevention Program, Rockville, MD. Available at: http://www.bsc.gwu.edu/dpp/slides.htmlvdoc.)

terms of physical activity achieved. In fact, the results were so overwhelmingly favorable for the intensive lifestyle group that it became necessary to terminate the study a year early. Average weight loss was 0.1 kg for the standard lifestyle group, 2.1 kg for the metformin group, and 5.6 kg for the intensive lifestyle group, with an average follow-up of 2.8 years (**Fig. 6**). The incidence of diabetes was 31% lower in the metformin group and 58% lower in the intensive lifestyle changes group compared with the standard lifestyle changes group. Interestingly, this contrast was even greater in patients older than 60 years of age on subgroup analysis (**Fig. 7**).

The DPP further emphasized the importance of diet and exercise in the prevention of diabetes by suggesting that it was more effective than even the first-line pharmacologic treatment of diabetes, metformin. In addition, in the posttreatment analysis of this study of the 1274 participants who had not developed diabetes, a repeat OGTT



**Fig. 6.** Mean weight change during DPP trial. The average follow-up time was 2.8 years, that is, the number of participants decreased during the course of the study. (*Courtesy of* the Diabetes Prevention Program, Rockville, MD. Available at: http://www.bsc.gwu.edu/dpp/slides. htmlvdoc.)

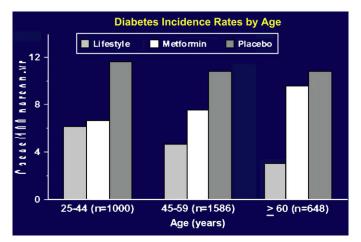


Fig. 7. Effectiveness of lifestyle compared with metformin in elderly. (*Courtesy of* the Diabetes Prevention Program, Rockville, MD. Available at: http://www.bsc.gwu.edu/dpp/slides.htmlvdoc.)

was performed after a washout period of 1 to 2 weeks off metformin.<sup>12</sup> After the washout, diabetes was diagnosed more in the metformin group than before the washout, suggesting that metformin was not truly preventing diabetes but instead really pretreating it. Although the authors state that there was still a 25% reduction compared with placebo in this group, we do not know if the reduction may have been smaller if they had used a longer washout period. It may be debated whether metformin alters the progression of the underlying disease process or is instead a pretreatment.

By contrast, exercise has been shown to clearly increase insulin sensitivity and alter the pathophysiological conditions underlying the development of diabetes. Exercise through muscle contractions increases translocation of GLUT4 transporters to the cell surface, increasing peripheral uptake of glucose. Exercise-mediated effects are insensitive to inhibitors of PI 3-kinase unlike insulin-mediated GLUT4 transport. In fact, exercise increases the amount of GLUT4 transporters locating to the cell surface in response to the same dose of insulin. Exercise also activates AMP (adenosine monophosphate)-dependent kinase (AMPK), which lowers Acyl-CoA levels and increases insulin signal transduction. Many of these effects of exercise can be seen independent of weight loss.

The benefits of exercise for adults in preventing diabetes are apparent in the recent publication of the 20-year follow-up data of the Da Qing Study.<sup>13</sup> In 1986, 577 adults with impaired glucose tolerance at 33 clinics in Da Qing City, China, were randomized by clinic site to a control, diet, exercise, or diet plus exercise group.<sup>14</sup> The diet group participants were prescribed a diet containing 25 to 30 kcal/kg body weight (105–126 kJ/kg), 55% to 65% carbohydrate, 10% to 15% protein, and 25% to 30%. They and were encouraged to increase their vegetable intake and decrease their alcohol and simple sugar intake. Overweight subjects (BMI  $\geq$  to 25 kg/m<sup>2</sup>) were encouraged to decrease their calorie intake to lose weight until they reached a BMI of at least 23 kg/m<sup>2</sup>. Patients received individualized counseling sessions with their physician and periodic small group counseling sessions. The exercise group was encouraged to increase leisure exercise by at least 1 unit a day, with 2 units for younger subjects. Units varied from 5 minutes of very strenuous exercise to 30 minutes of mild exercise (refer to **Table 1**). The exercise group also had periodic small group sessions, once

Table 1 Units of activity		
Intensity	Time (min)	Exercise
Mild	30	Slow walking, traveling by bus, shopping, housecleaning
Moderate	20	Faster walking or walking down stairs, cycling, doing heavy laundry, ballroom dancing (slow)
Strenuous	10	Slow running, climbing stairs, disco dancing for the elderly, playing volleyball or table tennis
Very strenuous	5	Jumping rope, playing basketball, swimming

Each example is 1 unit of activity that is, 30 min of mild exercise (slow walking) is equivalent to 5 min of very strenuous exercise (jumping rope)

Data from Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 1997;20:37–44.

weekly for the first 4 weeks, then monthly for 3 months, and then once every 3 months for the remainder of the study. The diet plus exercise group received both of these interventions. The 6-year data indicated that the cumulative diabetes incidence was 43% in the intervention group (with no significant difference between diet, exercise, or diet and exercise interventions) and 66% in the control group. The number needed to treat to prevent 1 case of diabetes was 6, and the intervention group after multivariate analysis had a 43% lower incidence of developing diabetes than the control group (hazard rate ratio, 0.57; 95% CI, 0.41-0.81).

During the 20-year follow-up, the cumulative diabetes incidence was 80% in the intervention group and 93% in the control. In addition, the participants in the intervention had an average of 3 to 6 fewer years with diabetes. However, it must be noted that the subjects in the intervention arm were 2 years younger on average at baseline, although there were no differences in other baseline characteristics, such as lipids, BMI, and fasting glucose. In 2006, there was no difference in the surviving participants in the intervention and control groups in terms of total calorie intake or the amount of leisure time physical activity when they were questioned about the preceding 1 year. The Da Qing follow-up study illustrates that the long-term effects of exercise can delay the progression to diabetes by a few years, although it may not prevent diabetes without sustained lifestyle changes, including continued exercise.

These are some of the trials that have led the American Diabetes Association to recommend for adults modest weight loss (5%–10% body weight) and regular physical activity through behavioral changes in lifestyle to prevent diabetes. However, one of the greatest difficulties that have been observed in weight loss trials has been a tendency to regain weight in long-term follow-up. Studies have shown that after being treated for 20 to 30 weeks with behavioral intervention adult subjects typically regain about 30% to 35% of their lost weight in the year following treatment.<sup>15</sup> Often at 5 years, these patients return to their baseline weights. In addition, data from studies of specific populations cannot always be extrapolated to a large diverse population base. When patients are enrolled in studies to lose weight, they are often given more structured individualized attention than resources allow in a community setting. In addition, many patients who are enrolled in studies are often either self-selected or selected through the study recruiters with an unintentional bias toward compliance.

Further obstacles to sustained weight loss and increased physical activity may be that this involves permanently altering behavioral patterns that are often established in childhood. If public health goals are to prevent obesity and type 2 diabetes, targeting the prevention of obesity in adulthood may be too late considering that one-third of adults in the United States are already obese. In fact, many adults learn about lifestyle changes only after being diagnosed with illnesses such as type 2 diabetes. Although the metabolic syndrome in children remains controversial,<sup>16</sup> most of the children who are obese tend to mature into obese adults. This has particular resonance in preado-lescence and adolescence. A longitudinal study demonstrated that two-third of the children who are obese at the age of 10 years and older are likely to become obese as adults.<sup>17</sup> The prevention of obesity in childhood would protect the advances that have been made toward decreasing human morbidity and mortality.

## THE RISKS OF CHILDHOOD OBESITY AND METABOLIC SYNDROME

The risks of childhood obesity are not limited to ensuing adult obesity. A recent study of 439 obese children considered several factors similar to those that define metabolic syndrome in adults.<sup>18</sup> Compared with a group of nonobese siblings, a significantly larger percentage of the obese subjects were found to have systolic/diastolic blood pressures (BPs) above the 95th percentile, triglycerides above the 95 percentile, high-density lipoprotein (HDL) levels less than the 5th percentile, and impaired glucose tolerance. Surrogate markers of inflammation such as C-reactive protein (CRP) and IL-6 were also elevated in the obese subjects. Adiponectin was decreased as can be expected in insulin-resistant individuals. In fact, in the 2-year follow-up of 77 of the study subjects, 8 out the initial 34 who met the authors' criteria for metabolic syndrome developed type 2 diabetes. Another cross-sectional study examined the guality of life of children through guestionnaires and found that obese children and adolescents reported a significant impairment in all aspects that were examined (including physical, psychosocial, emotional, social, and school functioning) in comparison with healthy children and adolescents.<sup>19</sup> In fact, the authors remark in their comments that "The likelihood of an obese child or adolescent having impaired health-related QOL was 5.5 times greater than a healthy child or adolescent and similar to a child or adolescent diagnosed as having cancer."

In adults, the likelihood of patients with impaired glucose tolerance or impaired fasting glucose progressing to diabetes is 25% over 3 to 5 years.<sup>20</sup> There are no large longitudinal studies on children with such data, but smaller studies on at risk populations suggest that there is a high likelihood of progression to type 2 diabetes.<sup>21</sup> Considering the current epidemic of obesity, it is surprising that recent data by the SEARCH for Diabetes in Youth study indicated a low overall prevalence of type 2 diabetes in children.<sup>22</sup> The study found that the overall prevalence of type 1 diabetes was much higher than the prevalence of type 2, with a 1.54 versus 0.22 prevalence per 1000 persons, respectively. However, there were significant ethnic variations when looking at children aged 10 to 19 years. Type 2 diabetes was only 6% of all diabetic cases diagnosed in non-Hispanic whites compared with 22% of all diabetic cases diagnosed in Hispanics. In American Indians, type 2 diabetes has overtaken type 1 in prevalence among children, a startling 72% of all cases of diabetes. The authors suggest that an underestimation of type 2 diabetes may exist considering the difficulties of accurate classification and prompt diagnosis, which is of particular relevance since the SEARCH data were obtained largely through chart review. If rates of obesity continue to rise, while US demographics are growing ethnically diverse, escalating rates of type 2 diabetes in childhood may become an increasing public health concern.

## THE DEFINITION OF CHILDHOOD OBESITY AND CONTRIBUTING FACTORS

Targeting childhood obesity is challenging as the very definition of obesity in childhood is controversial. Unlike the definition in adults that relies solely on absolute BMI, the

growth curve needs to be taken into account in children. The 2000 growth chart developed by the Centers for Disease Control and Prevention (CDC) is based on national height and weight data for children aged 2 to 19 years. Growth and height are therefore comparative to the reference population, and as charts are revised in the future, they may reflect an overall heavier population. In addition, the CDC and National Heart, Lung and Blood Institute have defined obesity in children as a BMI at or greater than 95% on the 2000 growth chart and overweight as greater than or at 85%. These definitions are arbitrary, and unlike the adult definitions of obesity and overweight, they are not based on health risk data.

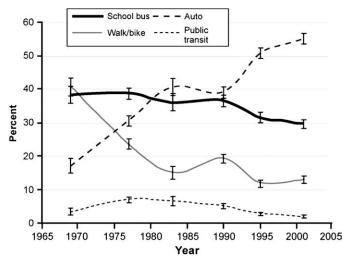
The prevention of childhood obesity must take into account factors that have contributed to the growing epidemic of obesity in children. Many of these factors may be similar to those that have contributed to the adult obesogenic environment, including the popularity of fast food, increased transportation by car, and the impact of television (TV) on leisure time. However, there may also be different factors that have contributed to the pediatric obesogenic environment specific to how children spend their time. These factors include how children play, what they do in school, and even changes in how and when they eat. But, similar to adult obesity, ultimately it is the equation of energy balance that becomes lopsided, with increased intake and decreased energy expenditure.

The importance of diet cannot be emphasized enough, but this review focuses on exercise in the prevention of childhood obesity and diabetes. In actuality, most obesity and diabetes prevention trials use a combination of exercise and dietary interventions, as it is necessary to account for both parts of the energy equation to yield meaningful results. Although it is commonly perceived that the culprits of the obesity epidemic are increased time spent by children watching TV and increased fast food intake with larger portion sizes, objective data are difficult to collect on what is likely a multifactorial cause. Social trend data would assist in determining which factors are likely to contribute to obesity, although not necessarily establishing a causal relationship. They would also assist in creating practical interventions to halt the current obesity epidemic.

Specific data are somewhat limited concerning these broad social trends. Survey data in 1997 data compared with those in 1981 indicated that children's free time overall decreased, with increased time spent outside the home, including at school and at day care.<sup>23</sup> Children spent less time eating meals as a primary activity, with more snacking and eating as a secondary activity. Surprisingly some of the survey data indicated that children spent less time watching TV largely due to less leisure time. There was more time spent in structured activities, especially for children younger than 9 years of age, resulting in less unstructured playtime. In terms of other media usage, TV remained the dominant medium overall, but in some groups, other trends emerged. For example, boys aged 8 to 13 years averaged 47 min/d playing video games. The survey data unfortunately did not account for how time was spent in school or at daycare, leaving large gaps in our knowledge base. However, it emphasized that children were spending increasingly longer amounts of time away from home in general. Another study examined transportation to school and found that physically active transportation (ie, walking or biking) to school fell significantly between 1969 and 2001, largely being replaced by automobile transportation to school (Fig. 8).24 However, the largest decline occurred between 1969 and 1983. Possible reasons for the decline cited by parents included increasing school distance, traffic, sidewalk coverage, fears of "stranger danger," and convenience.

According to CDC data on youth risk behavior for 2005, 21.1% of students used a computer for something that was not schoolwork for 3 or more hours on an average school day.<sup>25</sup> An even greater number of students watched TV, with 37.2% watching

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**Fig. 8.** Standardized mode shares for trips to school. Standardized to 2001 age and race distribution. Error bars represent the 95% confidence intervals. (*From* McDonald NC. Active transportation to school: trends among U.S. schoolchildren, 1969–2001. Am J Prev Med 2007 Jun;32(6):509–16; with permission.)

TV for 3 or more hours per day. In terms of attending gym class, only 54% went to gym class 1 or more days in an average week, and of those who went to gym class, only 84% actually exercised for longer than 20 minutes.

Some studies have focused on finding a direct relationship between factors in the environment and obesity. A randomized, controlled clinical trial found that reducing TV and computer use by 50% in the intervention arm reduced energy intake significantly compared with that in the control group, although there were no significant changes in age- and sex-standardized BMI or physical activity.<sup>26</sup> A cross-sectional study in 2004 including 878 adolescents in the Patient Centered Assessment and Counseling for Exercise Plus Nutrition Project or PACE program studied 7 dietary and physical activity variables and found vigorous physical activity of 60 minutes daily to be the only variable with an independent association with weight status for boys and girls.<sup>27</sup> Physical activity was assessed through the use of accelerometers. One major limitation was that dietary intake was assessed through 24-hour recall, and total calorie intake was actually lower in the overweight group, suggesting that there may have been underreporting in this group compared with normal weight adolescents.

## DIABETES OR INSULIN RESISTANCE PREVENTION IN CHILDREN

Unfortunately, there have not been large randomized, controlled trials comparable to the DPP or Finish Diabetes Study for diabetes prevention in children, considering the low incidence of type 2 diabetes in children. To examine such a primary endpoint, long-term follow-up into adulthood would likely be required. However, numerous smaller, randomized, controlled studies have addressed insulin resistance and inflammatory markers in children. There have been many more randomized, controlled trials addressing obesity prevention in children than in adults, as this has been a public health concern that some with foresight had anticipated as far back as 1979 (please refer to appendix 1 for overview studies).<sup>28</sup>

Several small, randomized, controlled trials have looked at metabolic parameters, including insulin sensitivity, cardiovascular fitness as measured by maximum oxygen consumption (VO<sub>2</sub> max), and body composition through either school-based or family-based trials. A randomized, controlled trial on largely first- or second-generation Dominican schoolchildren in New York studied 73 eighth graders who were randomized to either an intervention group that included diet and exercise sessions or the control for 3 to 4 months.<sup>29</sup> The intervention group received on average 14 sessions on nutrition focusing on lower fat intake, and students were given the option of dance or kickboxing classes 3 times a week instead of gym class. About 20 out of the 29 students in the intervention group elected to attend the exercise classes as opposed to regular gym class.

The authors found that CRP was significantly lower in the intervention group compared with that in the control group at the completion of the study. Following the intervention, the percentage of body fat, as measured by bioimpedance, BMI, and IL-6, was significantly lower in the intervention group compared with that in baseline testing. Notably, for both inflammatory markers, CRP and IL-6 differences were only significant for those in the intervention group that participated in both the nutrition sessions and the exercise classes. The quantitative insulin sensitivity check index, or QUICKI score, was higher compared with that in baseline testing in the intervention group, indicating increased insulin sensitivity. The control group did not show any significant changes from baseline testing. There was no significant difference between the groups or from baseline testing in the other factors studied, including lipid profiles, glucose, insulin levels, TNF-a, adipocyte complement-related protein of 30 kDa (adiponectin), and acute insulin response. Actual dietary intake and exercise measurements were not measured (particularly outside of the school setting) and may be confounding variables. Percentage body fat as measured by bioimpedance is affected by hydration state and is not as reliable as other standards such as DXA. However, the study did propose possible changes in physical education curriculum that may be more effective in improving insulin sensitivity compared with traditional gym classes.

Another randomized, controlled study similarly focused on lifestyle-oriented exercise classes compared with standard gym classes.<sup>30</sup> However, this study targeted only children who were already obese with a BMI above the 95% for age. This population was from a rural Wisconsin school compared with inner city students in the Rosenbaum study. The subjects who were randomized to the intervention received educational handouts and were placed in fitness classes of 45 minutes each, with 5 sessions every 2 weeks. These classes encouraged noncompetitive activities, such as walking and cycling, and had only 12 to 14 children per class. The classes increased movement time (42 minutes out of 45) by not having the children change clothes. By contrast, those subjects randomized to the control group participated in traditional gym class, with only 25 minutes of movement time and classes of 35 to 40 students.

The intervention group had significant improvements in VO<sub>2</sub>max compared with initial testing (P<.001) and with the control group. The intervention group also had significant decreases in both percentage body fat, as measured by DXA, and fasting insulin levels compared with those in initial testing. The intervention group had a significant rise in glucose-insulin ratios compared with baseline testing. There were no significant differences in BMI and fasting glucose level in the intervention group compared with those at baseline testing or control. There were no significant differences in the control group for all variables compared with baseline testing.

This study offered more specific changes that may be instituted in a physical education curriculum, with the goal of improving insulin sensitivity and cardiovascular fitness while decreasing body fat percentage. Although there was no decrease in BMI, other markers of physical fitness improved, emphasizing the benefits of increased exercise. Further studies are needed to evaluate the cost benefit for smaller gym classes, but other formats that increase active time (for example, not changing clothes) are easily implementable. In contrast to the Rosenbaum study, this study targeted obese children only. Although this may be financially more viable, the authors do not comment on any feelings of stigmatization the obese students may have felt toward being separated from their peers. Perhaps it is reassuring that 50 of the 55 students initially invited at the single school enrolled in the study, and only 3 students (5%) dropped out after randomization. However, for public implementation of similar programs this factor is important to consider and address.

Another study, Bright Bodies, also targeted obese students who were above a BMI percentile of 95% on the 2000 CDC chart.<sup>31</sup> Like the Rosenbaum study, this study targeted inner city youth but was family-based rather than school based. The study randomized 209 subjects aged 8 to 16 years in a 2:1 ratio to the intervention and control groups, with an initial further 1:1 randomization in the intervention group to meal structured versus better choices. The meal structured group was dissolved after a high dropout rate (83% of the 35 subjects), and these data were not included in the analysis. The intervention group exercised 50 minutes twice a week at a minimum, with nutrition or behavior classes for 40 minutes once a week for the first 6 months. These were attended by both the parents/caregivers and the children. The exercise classes varied but were high-intensity, including dance, basketball, and sports drills. Subjects wore heart rate (HR) monitors and were encouraged to reach 65% to 85% maximum HR. They were also encouraged to exercise 3 additional days at home per week. During the last 6 months of the study, exercise classes were decreased to twice per month. The control group received diet and exercise counseling twice during the study, at baseline and again at 6 months. The primary endpoint was a change in BMI at 6 months.

The intervention group had decreased BMI and percentage body fat as measured by DXA compared with baseline at 6 months and at 12 months, in contrast to the control group who had an increase in BMI and percentage body fat. Compared with controls, the intervention group also had a decrease in insulin resistance as measured by HOMA-IR scores (Homeostasis Model Assessment of Insulin Resistancecomputed by adding fasting insulin and fasting glucose levels and dividing by 22.5). There was a remarkable contrast between the control group whose BMI increased by 1.6 kg/m<sup>2</sup> (a net gain of 7.7 kg) and the intervention group whose BMI declined by 1.7 kg/m<sup>2</sup> (net gain of only 0.3 kg accounted for by an increase in height) during the 12-month period. The study had a high dropout rate even after excluding the arm that was dissolved, with only 119 of the 209 participants completing the study after 12 months. This high dropout rate after enrollment may have introduced some bias. Interestingly, the dropout rates were higher in the control group than those in the Bright Bodies group, which suggests that the intervention introduced practical methods for the subjects to increase activity. However, even with the significant dropout rate, the study was large enough to be adequately powered. In addition, the family-based approach likely yielded some benefits to the caregivers as well, although this was not studied.

Several smaller studies supported these results. One study looked at 15 obese adolescents (BMI >30 kg/m<sup>2</sup>) who were randomized to control or intervention for 3 months.<sup>32</sup> The intervention group had weekly nutrition sessions and 45-minute aerobic activity sessions 3 times a week (with 1 session per week monitored, with subjects' parents also participating). The exercise target was gradually achieved in

the first 2 weeks. The nutrition sessions focused on low-fat meals, portion control, and limiting soda intake. The intervention group was also encouraged to limit TV use. The control group gained weight, with an increased BMI and body fat percentage measured by DXA during the 3 months, whereas the intervention group maintained weight and BMI. The intervention group had a decreased body fat percentage. In addition, HOMA-IR, CRP, fibrinogen, and IL-6 were decreased in the intervention group compared with those at baseline. There were no significant differences in low-density lipoprotein (LDL), HDL, or triglycerides (TG). This study was quite small with only 7 subjects in the control arm and 8 in the intervention, but it supported the conclusion that increased physical activity improves insulin sensitivity in children.

The second was a Korean study that evaluated 44 obese girls with a BMI >95% based on the Korean Pediatric Association 1998 growth charts. Subjects were randomized to control or lifestyle plus exercise for 12 weeks.<sup>33</sup> The intervention group had supervised sessions of walking 10 minutes on Monday, Wednesday, and Friday and 40 minutes of walking on Tuesday, Thursday, and Saturday. The targeted intensity was 55% to 75% of maximum HR, and the girls wore heart monitors as well as pedometers. The lifestyle intervention included weekly behavior modification sessions with a trained counselor. Subjects kept dietary records in the control and intervention groups, but no significant differences were noted in total caloric intake or macronutrient content. The intervention group had a greater reduction in body weight, BMI, waist circumference, waist-to-hip ratio, systolic blood pressure (SBP), LDL, total cholesterol, glucose, insulin, TG, CRP, leptin, and HOMA-IR. No significant differences were observed in diastolic blood pressure (DBP), HDL, HbA<sub>1c</sub>, or adiponectin compared with those at baseline. This study showed increased insulin sensitivity in obese subjects after an exercise intervention in a population that is increasingly at risk, considering that Asian populations develop diabetes at a higher rate at the same BMI as that of Caucasian populations, with increased propensity for abdominal obesitv.

These trials have looked at methods to increase insulin sensitivity, which may delay or prevent the onset of diabetes. The Rosenbaum study was also useful in examining the prevention of obesity by focusing on a general population of children. The other trials mainly had outcomes that could be applied to obesity treatment but not directly to obesity prevention, which is a more immediate and growing public health concern.

## FAMILY-BASED OBESITY-PREVENTION TRIALS IN CHILDREN

Several questions arise while formulating obesity-prevention trials. For example, play has always been an essential component of childhood. Even when observing the animal kingdom, we see that young animals' play often models adult behavior. This was likely also true for humans in the premodern era, with children "playing" to fish and hunt while actually learning these skill sets. Children often follow the behaviors of other adults in the community, parents, or caregivers. In the modern world, if children see parents or caregivers using computers frequently even at a young age they desire to imitate them with toy laptops. It is highly likely that sedentary play may lead to decreased physical activity patterns in adulthood. Family-based approaches, where children spend time with parents, increasing physical activity and fitness together, may be more likely to succeed. Even in school-based approaches, without family involvement, the child may feel isolated or be challenged to maintain lifestyle changes in an obesogenic home environment. This possibility has not been addressed in many school-based studies, because activity is often not objectively measured outside the school environment.

Most obesity-prevention trials have been school based, as these are easier to design and implement. However, some family-based trials for obesity prevention have attempted to show that this is another effective approach. A Colorado-based trial focused on a simplified intervention (encouraging an increase in steps per day and cereal consumption) as part of a larger initiative termed America on the Move.<sup>34</sup> The study randomized families who had at least 1 overweight, 8- to 12-year-old child, with a BMI greater than or equal to 85% for age, to control (n = 23) or intervention (n = 82). The intervention group was encouraged to increase steps per day from baseline data to a goal of an additional 2000 steps per day as measured by a pedometer and to eat 2 servings of cereal a day for the 14-week intervention period. The control group also wore pedometers, but the display was turned off, thus not offering feedback. The intervention group increased cereal consumption compared with control but was unable to reach the target of 2 servings per day. In self-reported dietary data, there was no difference in macronutrient intake or total calorie intake between the groups as a result of the intervention.

There was a significant increase in steps approaching an additional 2000 steps in the intervention group compared with that in the control group. There was a decrease in BMI and percentage body fat in the intervention group compared with that in the control. However, when this was analyzed based on sex-specific data, significant decreases in BMI and percentage body fat, as measured by multiple-site, skinfold thickness, were evident only in the girls in the intervention group and not in the boys. Interestingly, this sex-specific difference was also present in the parents, with mothers in the intervention group having significantly decreased BMI and percentage body fat compared with control. The fathers demonstrated a significant difference from baseline (although not control) in change in percentage body fat, which was not evident in the boys.

These sex-specific differences are likely attributable to the design of the study. There was a much larger intervention group (n = 82) than control group (n = 23), which may have caused the study to be underpowered, in particular failing to show a significant difference in the boys (only 8, or 73%, of the control boys completed the study compared with 12, or 86%, of the control girls finishing the study). Because of the small size of the study group, the results of a subgroup analysis may not be valid. Another possibility is that since the boys in the intervention group had an increased number of steps compared with those in the control group, the measurement of percentage body fat by skinfold thickness as a follow-up measure may not be as accurate in young boys as in other populations. The use of skinfold thickness itself lacks the accuracy of other methods in measuring percentage body fat, especially following exercise interventions. A method such as DXA would be preferable, albeit more expensive. Although the study was limited, it demonstrated that children, particularly preadolescents, are capable of increasing their activity levels without specific structured activities. This is especially true with family support and participation. It allows the flexibility for families to pursue activities they enjoy without a regimented approach, leading to an increase in physical fitness.

Another similar family-based study also used pedometers to encourage physical activity but with an open-loop feedback system.<sup>35</sup> Open-loop feedback as opposed to closed-loop feedback involves the participation of a human being, in this case, most likely a parent or other family member, to reinforce certain behaviors. This study randomized children aged 8 to 12 years with a BMI less than 90%, who watched TV or played video games for 15 hours or more per week, to either an open-loop feedback plus reinforcement group or a control group for 6 weeks. The intervention group was encouraged to be physically active and was given TV/video game time based on their

activity levels, which was measured by pedometers. About 400 activity units (walking for about 1 hour at 3 mph) were equal to 60 minutes of TV/video game time. Television access was controlled by the caregiver, based on allowance from physical activity units. As in the Colorado study, the control group also wore pedometers but with the display turned off. In this study, the control group was also encouraged in a weekly counseling group to have moderate to vigorous activity for 60 minutes daily. There was no change in BMI z-scores (standard deviations from values that are 50% for sex and age) between the intervention and control groups in the 6-week period of the study. However, physical activity in the intervention group increased by 24% compared with baseline and 32% compared with control, a significant difference. Although the study did not show significant changes in BMI during a relatively short intervention period, it did show increased activity levels that may contribute to obesity prevention in the long-term.

These obesity-prevention trials have attempted to increase unstructured active playtime, because some social trend data have suggested that unstructured playtime has decreased in the past 30 years, especially for younger children. Yet unstructured playtime, to be meaningful, may require space, good weather, safety, and play companions. For example, the 2 family-based studies discussed previously<sup>34,35</sup> were conducted in Colorado and Buffalo, NY, respectively. It is a distinct possibility that the steps taken daily may vary seasonally, with probably less steps being taken during winter as opposed to summer. Additionally, learning structured skill sets may be valuable, as these can be carried on through puberty into adulthood, resulting in a continuum. We speculate that both unstructured and structured playtimes are equally important, with the use of pedometers and open-loop systems being used in younger children and structured activities or sports playing a larger role in older children.

## SCHOOL-BASED OBESITY-PREVENTION TRIALS IN CHILDREN

In contrast to these limited family-based trials, a much larger number of trials have been designed as school based. The reason for this becomes evident in that schools offer an easily accessible system already in place for instituting programs. Indeed, other models of school-based interventions, such as smoking cessation, have had considerable success. However, school-based programs also face drawbacks, such as lack of continuity during summer break, the stigmatization of singling out from peers in programs that target only overweight individuals, and the possible lack of family support or knowledge.

As mentioned in the earlier chapter, the Planet Health study randomized schools with a total of 1295 children participating in grades 6 to 7 to either intervention or control for a period of 21 months.<sup>36</sup> The intervention schools taught 16 core lessons focused on 4 behavior modifications, including decreasing TV time, increasing fruit and vegetable consumption to greater than 5 servings per day, decreasing fat intake, and increasing physical activity. The intervention was largely educational with no specific instructions for physical activity. Physical activity and dietary intake were measured through survey data. The intervention group had significant decreases in obesity prevalence (as measured by BMI percentile and triceps skinfold thickness) compared with those in control schools. However, in boys there was no difference between the intervention and control groups. In terms of secondary endpoints, both boys and girls reported a decrease in TV viewing time. The girls in the intervention group also reported a significant decrease in controls. The study was limited

by self-reported data that may have been subject to over- and underreporting. Interestingly, the study found sex-specific differences favoring girls as opposed to boys similar to the Rodearmel study. However, this study was much larger with control and intervention numbers relatively equal (intervention n = 641 and control n = 654). The study suggested that girls are more likely to decrease their dietary intake in response to a behavioral approach. This may be influenced by media emphasis on thinness and dieting, particularly in teenage girls. Although the authors noted that there was no evidence for increases in extreme dieting behaviors among the girls, many adolescents with eating disorders mask their behaviors. Further studies would need to be performed to address these concerns. The Planet Health Study indicated that behavior modification programs may be a useful tool in obesity prevention by decreasing dietary intake. Physical activity did not change between the intervention and control groups based on survey data. A more directed and activity-oriented approach may be required for initiating exercise.

Another large, randomized, controlled trial was conducted in American Indian school children.<sup>37</sup> a high-risk population not only for obesity but for progression to type 2 diabetes of childhood as indicated by SEARCH data. The study randomized 1704 children from third through fifth grade to a Pathways intervention or control for 3 years. The Pathways intervention included weekly nutrition lessons and dietary advice provided to school cafeterias for meal planning. It also included take-home information as well as events for families to attend to bolster family involvement. In terms of physical activity, the Pathways intervention had a minimum of 3 30-minute physical education classes per week with moderate to vigorous activity based on the SPARK program and additional exercise breaks during class for 2 to 10 minutes. There was no change in BMI percentile, % body fat, as measured by bioimpedance, or triceps and subscapular skinfold thickness between the groups. A 24-hour recall showed a significantly lower total and percentage of fat intake in the intervention group. Physical activity as measured by random 24-hour sampling of 15 students in second grade (at baseline) and again at fifth grade showed no difference between the 2 groups.

Interestingly, random sampling accelerometer data did not match with self-reported data, which indicated increased physical activity. Children may have been overreporting activity levels. As seen in overweight adults, overweight children may also underreport intake and may have been more tempted to do so after an intervention emphasizing the importance of healthy eating. One explanation for why the study failed to detect a significant difference in endpoints could be that bioimpedance and skinfold thickness lack adequate accuracy to determine differences in body fat percentages in growing children. An alternative explanation may be that the school did not offer 60 minutes of moderate to vigorous activity per day as suggested by the PACE study. In practical terms, this may be difficult to achieve entirely during school while balancing time for other academic requirements. That the children did not change their physical activity outside of school was likely a confining factor. In addition, there may be ethnic differences in this study population that limit generalizability. The study did not address any change in insulin sensitivity the children may have had, but this may have been a more important and immediate endpoint in this group at high-risk for the development of type 2 diabetes.

Several other large-scale, randomized, controlled trials failed to show a difference between intervention and control groups in the prevention of obesity. A British study performed in Leeds randomized 10 schools to intervention in the active programme promoting lifestyle education in schools (APPLES) program or control for 1 year.<sup>38</sup> The APPLES program was a behavioral modification program, which was designed

to target the entire school community, including parents, teachers, and catering staff. It was based on school action plans developed by the individual schools on the basis of their perceived needs. The study had 636 children aged 7 to 11 years and showed no change in BMI or levels of physical activity as measured by questionnaire. There was, however, a significant increase in vegetable consumption based on 24-hour recall in the intervention group compared with that in the control. However, it is unclear in the study how much the intervention differed between the schools in the intervention arm. In addition, there was no direct implementation of increased physical activity during school as far as can be assessed by published data.

Another behavioral study, the Wise Mind Project randomized schools to either a Healthy Eating and Exercise or to a Alcohol/Drug/Tobacco abuse prevention program.<sup>39</sup> The intervention was mainly educational, although teachers were provided with Physical Activity Centers with balls, beanbags, jump ropes, and balloons to encourage indoor and outdoor play during recess. The study had 670 subjects in second to sixth grade and showed no significant differences between the groups in the primary endpoint, z-BMI. There were also no significant changes in secondary endpoints, including body fat percentage as measured by bioimpedance, physical activity as measured by questionnaire, or total calorie intake as measured by digital photography of food leftover on meal plates. The authors suggest that the study was underpowered and thus unable to detect a difference. However, the study did show significant differences in psychosocial variables, another secondary endpoint. The interventional arm had greater self-esteem, less depression, and fewer eating disorder symptoms at the completion of the study compared with those in control as measured by questionnaire.

Another large population-based study adopted an environmental approach rather than a mostly educational one. This study randomized schools with mean enrollments of 1109 students in grades sixth through eighth to an intervention, Middle School Physical Activity and Nutrition program, (M-SPAN), or control for a period of 2 years.<sup>40</sup> The intervention included daily physical education classes and encouraged increased physical activity outside of class as well. Nutritional changes were made in school cafeterias to offer more low-fat choices. In addition, a main component of the program was instituting policy change, which was initiated through health policy meetings and student health committees. There was parental education through newsletters and parent-teacher association meetings and school incentives to participate. Data were collected on food intake and physical activity through direct observation on a random sample. Survey data were collected for out-of school information.

The study found greater physical activity as observed in school in boys in the intervention group compared with that in control but no significant differences in girls. This was also true for out-of school activity. There were no significant differences in total fat intake or saturated fat intake. Unfortunately, BMI was not measured in this study but was self-reported. BMI declined for boys and not for the girls according to selfreported data. Interestingly, this study also found sex-specific differences but the opposite of those found in Planet Health. The possible reasons for this may have been increased self-consciousness by girls during observation while exercising. It is unclear if the physical education classes in this study were coed, another factor that could have influenced the behavior of both boys as well as girls. The study was significantly limited by not gathering objective data in terms of BMI. The study did offer a different perspective in creating a school environment that was more conducive to a healthy lifestyle, which may have facilitated increased physical activity, especially for boys. The study attempted to alter the school environment to be less obesogenic, although significant environmental forces outside of school remained unaffected. Another school-based study took an academic and educational approach, randomizing 1013 fourth and fifth graders to intervention or control.<sup>41</sup> The Wellness, Academics and You, or "WAY" program integrated healthy behaviors into the academic curriculum by teaching 7 modules in subjects as diverse as language, mathematics, and science. The program had 10-minute aerobic exercise routines before the breaks during class in the interventional group. The interventional group had a 2% reduction in overweight (or BMI greater than 85%), but the authors state there were no significant changes in reported physical activity levels or nutritional uptake. There was a trend toward increased activity and increased fruit and vegetable consumption. The study could not determine the actual factors that resulted in the weight loss, but it offered a possible solution for schools in balancing time for academics and physical fitness. In fact, survey data from the teachers indicated improved attention and focus from the students in the interventional arm.

Perhaps these studies indicate that a combination of environmental, behavioral, and educational components is necessary for meaningful results in obesity prevention. Some limitations of many of these studies have been a lack of objective data with regard to actual physical activity performed, perhaps better gathered through accelerometer data, and dietary intake. It is possible that more structured interventions that increase physical activity, such as those performed in the Bright Bodies or Carrell studies, may ease student initiation toward becoming more physically active.

A 3-year randomized, controlled, international study in Beijing, China, in 2007 reported remarkably large decreases in obesity prevalence.<sup>42</sup> The study randomized primary schools (grades 1–4) to intervention or control, with a total of 2425 students. The study was conducted over 3 years. The intervention consisted of nutritional lectures with handouts once per semester for parents and didactic lessons every 2 weeks for the children in school on topics related to obesity prevention. In addition, there were interactive meetings for the parents of overweight or obese children once per semester as well as separate meetings for the overweight children. Mondays through Thursdays, overweight children and those children who failed physical education were asked to run for 20 minutes after class and were monitored. BMI was measured and calculated with age-specific and sex-specific percentiles, as recommended by the International Obesity Taskforce.

At the end of the study, the intervention schools had significantly lower overweight prevalence rates than those in the control schools, a 26.3% decrease compared with 14.3% increase. Obesity prevalence decreased in the intervention arm 32.5% compared with an increase in the control arm of 15.7%. This study showed startling differences in obesity outcome rates in contrast to other studies. Some factors that may have led to increased success rates in this trial may be that it was longer in duration, involved younger children, and involved significant parent participation. In particular, nutritional recommendations concerning meal preparation for the parents may have had a significant effect, perhaps amplified by differences in Chinese dietary habits. The study authors also noted that cultural differences may have contributed to overfeeding in single-child households (as most households are in China), with boys being overweight or obese at higher rates than girls. The study interventional arm specifically addressed this behavior, which may have had a significant effect on decreasing calorie intake. In addition, this study had a dramatically different ethnic composition than the prior American and European studies mentioned, which may have played a significant role.

In an effort to concentrate resources, the Chinese study targeted obese and overweight children, as did many of the other obesity-prevention studies. It is unclear if children felt stigmatized by this separation. In addition, with a rapidly increased percentage of the population at risk for obesity, it may be self-defeating not to address obesity prevention in the general population. One challenge with population-based programs, however, is ensuring safety. Would thin children be at risk for losing weight or having a deceleration in growth? In the study by Jiang and colleagues,<sup>42</sup> children in the intervention group and the control group had similar linear growth velocities. Many of the other trials noted that there were no adverse effects reported as a result of the intervention. The Pathways study identified children below the third percentile in growth velocity and referred them to their primary care provider, but it also noted that this number did not change as a result of the intervention.

As the American environment has grown more obesogenic, media images of what is considered attractive have trended in the opposing direction. This is particularly true in the case of women where advertisements routinely feature females who are underweight, with a BMI less than 18 kg/m<sup>2</sup>. In this social context, an important question is whether programs designed to prevent diabetes or obesity through increasing physical activity and discussing food choices would place teenage girls or other high-risk populations at risk for eating disorders. This situation is similar to one that has already been encountered in adolescents with type 1 diabetes. A cross-sectional study of 356 girls with type 1 diabetes found a higher prevalence of eating disorders, including bulimia, compared with controls without diabetes.<sup>43</sup> Some reasons for this may be increased weight gain after the initiation of insulin and the intensified focus on food choices necessary for the management of diabetes.

Some of the randomized, controlled trials addressed this concern. Authors of the Wise Mind Study found a decrease in the risk of eating disorder behaviors following the intervention. A school-based study called New Moves tried to minimize self-consciousness for adolescent girls while participating in physical education by offering girls-only classes.<sup>44</sup> Indeed self-consciousness in adolescent girls may be one reason the M-SPAN study observed a decrease in physical activity in girls compared with that in boys during school. A recent study using accelerometer data indicated that moderate to physical activity decreases between the ages of 9 to 15, with girls being less active than boys.<sup>45</sup>

The New Moves Program was advertised as a program to increase physical activity and help with healthy weight management. The intervention group received girls-only classes 4 days a week, which included noncompetitive activities, such as aerobic dance, yoga, and kickboxing, rather than traditional coed gym classes as in the control group. There was also 1 weight training session a week, with a nutrition/social support session every other week. Although the intervention group showed no significant changes in BMI at the end of the study, the program seemed to have a positive impact and was well received by the students.

As children have growing academic demands and greater time spent away from home, an alternative approach may be afterschool programs. The Georgia FitKid project was designed to increase moderate to vigorous physical activity after school.<sup>46</sup> The study randomized schools to either intervention or control, with 601 third graders participating for 1 year. The intervention was for 2 hours after school in which the first 40 minutes were spent assisting children with homework. They received a snack during this period following United States Department of Agriculture USDA guidelines for nutritional content. This was followed by an 80-minute period of exercise, which had 40 minutes of moderate to vigorous activity, with games such as tag, basketball, and soccer. About 5% of subjects wore HR monitors during the sessions. There was a significant decrease in percentage of body fat as measured by DXA in the intervention group as compared with the control. In addition, there was a significant improvement in cardiovascular fitness (as assessed by HR in

Appendix 1				
Study Name and Type	# of Subjects, Age, Population, and Length of Study	Diet Intervention	Exercise Intervention	Outcome
Rosenbaum et al School-based	73 eighth graders First- or second- generation Dominicans in New York City 3–4 mo	14 nutrition sessions	Dance or kickboxing 3 times a week instead of traditional gym class	<ul> <li>↓ CRP intervention vs control</li> <li>↓ % body fat (BF) by bioimpedance,</li> <li>BMI, and IL-6 intervention group vs baseline testing</li> <li>↑ QUIKI score intervention vs control</li> <li>No Δ lipid profiles, glucose levels, insulin levels,</li> <li>TNF- α, adiponectin, and acute in sulin response to glucose</li> </ul>
Carrel et al School-based	50 obese middle school children Rural Wisconsin School 9 mo	Educational handouts	Smaller fitness classes instead of traditional gym, 5 times in a 2-wk period	↑ VO <sub>2</sub> max intervention vs baseline and control ↓ % BF by DXA, fasting insulin, glucose-insulin ratios vs baseline No Δ BMI and fasting glucose
Savoye et al "Bright Bodies" Family-based	209 obese children ages 8–16 y Inner city population 6–12 mo	Intervention group— nutrition/behavior classes 40 min/wk for 6 mo and then every other week Control group—diet and exercise counseling twice during the study	High-intensity exercise classes 50 min twice a week at a minimum for 6 mo, then twice per month	<ul> <li>↓ BMI percentile, BF % by DXA intervention vs baseline</li> <li>↓ HOMA-IR intervention vs control</li> <li>↑ BMI percentile, % BF by DXA control vs baseline</li> </ul>
Balogopal et al Family-based	15 obese adolescents 3 mo	Weekly nutrition sessions	45-min aerobic activity sessions 3 times a week (with 1 session per week monitored)	<ul> <li>↓ BF % by DXA intervention vs baseline and control</li> <li>↓ HOMA-IR, CRP, fibrinogen, and IL-6 intervention vs baseline</li> <li>↑BMI percentile and % BF by DXA control vs baseline No Δ in LDL, HDL, or TG</li> </ul>
Park et al School-based	44 obese girls Ages 13–15 y Korean city population 12 wk	Weekly behavior modification sessions with a trained counselor	Supervised sessions of walking 10 min Monday, Wednesday, Friday and 40 min Tuesday, Thursday, Saturday, Sunday	<ul> <li>BMI percentile, waist circumference, waist/hip ratio, SBP, LDL, total cholesterol, glucose, insulin, TG, CRP, leptin, and HOMA-IR in intervention vs control</li> <li>No Δ DBP, HDL, HbA<sub>1c</sub>, or adiponectin</li> </ul>

Appendix 2				
Study Name and Type	# of Subjects, Ages, Population, and Length of Study	Diet Intervention	Exercise Intervention	Outcome
Rodearmel et al "America on the Move" Family-based	105 families with at least 1 overweight child aged 8–12 y Fort Collins area, Colorado 13 wk	Consumption of 2 servings of cereal a day	increase steps per day from baseline data to a goal of an additional 2000 steps/day as measured by pedometer	<ul> <li>↑In steps approaching an additional 2000 steps in intervention group vs control</li> <li>↓ BMI percentile and % BF by skinfold thickness intervention vs control</li> <li>On further sex-specific analysis</li> <li>↓ BMI and BF % was seen only in girls, not in boys</li> </ul>
Roemmich et al "Open-Loop Feedback" Family-based	18 families with children aged 8–12 y with BMI <90% who watched TV/played video games for ≥15 h/wk Buffalo, NY 6 wk	None	Intervention group— TV/video game time given based on activity levels measured by pedometers Control group— weekly counseling group to encourage moderate to vigorous activity for 60 min daily	↑ Physical activity in the intervention group vs baseline and control No Δ in BMI z-scores
Gortmaker et al "Planet Health" School-based	10 schools with 1295 children grades 6–7 Ethnically diverse communities in Massachusetts 21 mo	Lessons emphasizing ↑ fruit and vegetable to >5 servings per day, and ↓ fat intake	Lessons emphasizing ↓TV time and ↑physical activity	<ul> <li>BMI percentile and BF % by kinfold thickness intervention vs controls</li> <li>Sex-specific analysis showed no difference in boys</li> <li>TV time based on survey data fo boys and girls</li> <li>Energy intake in girls based on survey data intervention vs control</li> <li>Fruit and vegetable consumption in girls based on survey data intervention vs control</li> </ul>

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Callerbero et al "Pathways" School-based	1704 children third through fifth grades American Indian schools in Arizona, South Dakota, and New Mexico 3 y	Weekly nutrition lessons Dietary advice provided to school cafeterias for meal planning Take-home information and events for families	Minimum of 3 30-min gym classes per week based on the SPARK program Additional exercise breaks during class for 2–10 minutes	No ∆ BMI percentile, % BF as measured by bioimpedance or skinfold thickness ↓ Total and percentage of fat intake by a 24-hour recall in intervention vs control
Sahota et al School-based	10 schools with 637 children aged 7–11 y Leeds, England 1 y	A behavioral modification program "APPLES" targeting parents, teachers, and catering staff. Based on school action plans developed by the individual schools	Behavioral modification program "APPLES"	No ∆ in BMI, no ∆ physical activity as measured by questionnaire ↑In vegetable consumption based on 24-h recall in the intervention vs control
Williamson et al "Wise Mind Project" School-based	4 private Catholic schools with 670 students in second to sixth grade Louisiana 2 y	Educational program using posters, handouts, displays Wise Mind staff works with cafeteria on improving school lunches	Teachers given physical activity centers to encourage indoor and outdoor play	No Δ z-BMI or BF % by bioimpedance No Δ physical activity as measured by questionnaire or calorie intake as measured by digital photography of food leftover on meal plates
Sallis et al School-based	48 schools with 1109 students grades sixth through eighth San Diego County, CA 2 y	More low-fat choices in school cafeterias	Daily physical education classes Physical activity outside of class encouraged	<ul> <li>↑ Physical activity as observed in school in boys in the intervention vs control</li> <li>No ∆ in physical activity as observed in girls</li> <li>No ∆ in total fat intake or saturated fat intake as observed by random sample observation</li> <li>BMI was not measured</li> </ul>
				(continued on next page)

Appendix 2 (continued)				
Study Name and Type	# of Subjects, Ages, Population, and Length of Study	Diet Intervention	Exercise Intervention	Outcome
Spiegel and Foulk "The WAY program" School-based	1013 fourth and fifth graders Delaware, Florida, Kansas, North Carolina 5–6 mo	Educational module on nutrition	Educational module on designing basic workout routines 10-minute aerobic exercise routines before the breaks during class	↓ Reduction (2%) in overweight intervention vs control No Δ in reported physical activity levels or nutritional uptake
Jiang et al School-based	Primary schools (grades 1–4) with a total of 2425 students Beijing, China 3 y	Nutritional lectures for the parents 1x/semester Lessons and handouts every 2 wk for the children	Run for 20 min after class twice a week	↓ Overweight prevalence rates intervention vs control
Neumark-Sztainer et al "New Moves" School-based	6 schools with 201 girls Twin cities area, Minnesota 16 wk	Nutritional sessions every other week	4 d a week fitness sessions instead of traditional gym class, included weight training weekly, community guest instructors, lifestyle- oriented activities	Νο Δ ΒΜΙ
Yin et al "Georgia FitKid Project" Afterschool program	18 schools with 601 third graders Georgia 8 mo (data published) Study ongoing, planned for 3 y	Afterschool snack following USDA guidelines	80 min period of exercise, which had 40 min of moderate to vigorous activity	Using subjects who attended $\geq 40\%$ sessions— $\downarrow$ BF % by DXA in $\downarrow$ HR in response to 3-min bench stepping test $\uparrow$ bone mineral density in intervention vs control No $\Delta$ in BMI, blood pressure, and lipid profiles Using intention to treat analysis no $\Delta$ in any of the endpoints

response to 3-minute bench stepping test) and bone mineral density in the intervention group compared with the control. There were no significant differences in BMI, BP, or lipid profiles. However, this was based on data that only included children who attended more than 40% of the sessions (182 out of the initial 312 in the intervention group). When the data were reanalyzed using intention to treat, there was no significant difference. Perhaps this indicates that the method used in the study may have been effective at preventing obesity, but the practicality of afterschool programs is open to questions, particularly when considering barriers to attendance. Some of these may include difficulty with transportation and other conflicting afterschool commitments.

However, the Georgia FitKid program was largely designed to increase activity during a time of day that might have been spent in largely sedentary activities for many kids, such as watching TV after school. Indeed in this age of technology, TV, the Internet, and videogames are increasingly blamed for contributing to the rise in obesity. Yet these increasingly pervasive technologies are difficult to avoid. One possible solution would be to use technology to increase activity. The use of pedometers as useful technological devices in obesity prevention has been demonstrated, as discussed in prior studies. An innovative, randomized, controlled study designed a program that creatively used a videogame, pedometer, and parental involvement to increase activity.<sup>47</sup> The study randomized children aged 9 to 11 years to a futuristic videogame called MetaKenkoh or to control. The game involved accumulating steps on a pedometer, which were then downloaded into the program. The steps permit the child to continue progressing in and playing the videogame. Analysis of preliminary data indicated after 1 week that the intervention group had increased activity compared with baseline, whereas the control group had a drop in steps. Continued interest in the game as well as duration of interest remain to be determined. However, such an approach may be useful in combining active approaches to mainly sedentary activities. This may be likened to the expenditures that occur while playing videogames such as Wii Fit.48

## SUMMARY AND RECOMMENDATIONS

Most of the randomized, controlled studies addressing prevention of obesity in children do not show a decrease in BMI. Programs that have significant increases in moderate to vigorous physical activity during monitored sessions or as measured by objective data seem to show the greatest benefits. Although they do not often result in a significant decrease in BMI, most trials that use accurate measures have reported a significant decrease in percentage body fat. These trials have also shown improvements in markers of insulin resistance and inflammation through physical activity. The benefits of exercise thus extend beyond weight loss. Exercise alters the distribution of fat by decreasing visceral obesity. In addition, it contributes to increased insulin sensitivity and decreased inflammation. Perhaps focusing on obesity prevention as an endpoint is misguided, and studies should be designed to increase fitness and healthy eating. Focusing on fitness may demonstrate more immediate results and initiate lifestyle changes in subjects. This would embody a positive rather than a negative approach and in the long-term decrease overall rates of obesity.

Consensus Guidelines from 2005 have recommended that schools have 30 to 34 minutes of strenuous activity daily and that, in general, sedentary activity should be restricted.<sup>49</sup> In 2008, published guidelines from the Endocrine Society have recommended that clinicians recommend 60 minutes of daily moderate to vigorous physical

activity for children.<sup>50</sup> In addition, they also recommend limiting screen time to 1 to 2 hours daily. Although citing several studies to support these recommendations, both guidelines concur that there are limited quality data provided by obesity-prevention studies. However, they also state that lack of conclusive data should not preclude action toward obesity prevention.

One conundrum in designing randomized, controlled trials for the prevention of obesity and its associated complications is the issue of achieving a balance between an adequately powered study and one that also has accuracy. To have statistical significance and be adequately powered as well as to be considered a true population study, a large number of subjects are required. However, this often results in poorer measures of outcomes, with less objective data collected. Often studies will rely on survey data rather than direct measurement of physical activity, such as the use of an accelerometer, because they are less expensive and time consuming. Similarly, measurements of body fat percentage in many large trials have relied on skinfold thickness or bioimpedance, which is less accurate than DXA. Another barrier has been the significant duration of time needed to show treatment differences, especially in reduction of BMI.

Finally, rather than focusing on 1 type of intervention, multiple interventions are needed depending on the age, environment, and risk factors for the child. Younger children may benefit from more unstructured play and adolescents may benefit from programs that offer activities that will be available in the community as they transition to adulthood. School-based interventions could be implemented together with family-based involvement, such as evening sessions or parental monitoring of accelerometer usage. Resources could be allocated to design high-intensity interventions, such as the Bright Bodies program, to address populations most at risk for the complications of obesity, such as the American Indian population. Further funding could be broadly distributed in low-cost interventions to revise existing physical education programs. Some low-cost interventions might include increasing actual activity time, perhaps by separating girls and boys or by not having children change clothes.

Interventions to increase exercise should lay the foundations for a healthy lifestyle that can be maintained throughout adulthood. This will, in turn, result in healthier pregnancies, parenting, and in turn teach the next generation these same behaviors.

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