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HEALTHY

Prevention Study Group
Primary Prevention Trial

PROTOCOL

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1 EXECUTIVE SUMMARY AND OVERVIEW

In response to increases in incident cases of type 2 diabetes in American children and youth, NIDDK has funded a multi-site primary prevention trial designed to moderate risk for type 2 diabetes in middle school aged children. In pilot studies, it was found that an indicator of adiposity, a body mass index greater than the 85th percentile for gender and age, is the most prevalent, modifiable risk factor for diabetes in this age group. In addition, indicators of insulin resistance and dysglycemia, elevated mean fasting insulin and glucose levels, can be assessed to determine if the intervention is capable of reducing these risk factors for diabetes in middle school aged children.

The trial is conducted at 7 field centers in 42 middle schools randomly assigned to intervention or control. Following student recruitment and baseline data collection in the first semester of 6th grade (2006), the intervention is implemented in the second semester of 6th grade (2007) and continues throughout 7th (school year 2007-2008) and 8th (school year 2008-2009) grades. All students are exposed to components of the intervention, which are implemented school-wide or grade-wide; however, only students who provide appropriate informed consent and assent participate in data collection and evaluation. The primary objective of the trial is to determine if, at the end of the 8th grade, the intervention significantly impacts the risk for developing type 2 diabetes compared to control.

Six pilot studies were performed to collect data to guide the development of an intervention (see appendix 14.2). The prior studies focused on:

- Establishing the feasibility of recruiting students and obtaining physical and physiological measurements, including fasting and 2-hour post glucose load blood draws (early 2003).
- Evaluating a physical education (PE) class program designed to increase moderate-to-vigorous physical activity (late 2003).
- Testing the ability of a nutrition intervention to change food and beverage offerings in school food service and vending (early 2004).
- Implementing a program that integrated the PE class and food service nutrition interventions with a communications and awareness campaign (fall 2004).
- Determining the feasibility of a behavior change intervention, delivered through in-class and other school settings and family outreach, to accomplish self monitoring and goal setting (fall 2005).
- Evaluating PE class activities targeting 7th and 8th graders and a training and support program to motivate PE teacher buy-in and adherence (fall 2005).

Formative research has been conducted to inform the creation of all intervention components.

Based on a comprehensive review of the literature and the pilot study results, a robust multi-component intervention has been developed that impacts the environment and lifestyle choices of middle school children. The intervention consists of the following integrated components:

- changes in the nutritional quality of food and beverage offerings throughout the total school food environment, including cafeteria meals and programs, a la carte, and vending machines;
- changes in the physical education (PE) program, equipment, and teacher training to increase both participation and number of minutes spent in moderate-to-vigorous physical activity when implemented by PE teachers in PE class;
- brief classroom activities designed to increase knowledge, enhance decision making skills, promote peer involvement and interaction, and enhance social influence;
- individual and group behavior change initiatives aimed at promoting healthier behaviors through self monitoring, goal setting, and problem solving;
- family outreach to involve parents/guardians and family members by providing information and strategies to support youth in accomplishing behavioral goals; and

- school-wide communications to enhance and promote changes in nutrition, activity, and behavior.

In addition to the primary objective of affecting risk for T2D, major secondary objectives are to: further understand and characterize the etiology of risk of T2D in this age group; evaluate the ability of the intervention to influence lifestyle changes and choices both in and out of school; determine the cost-effectiveness of the intervention; compare academic performance, attendance, and comportment in intervention versus control schools; and describe the influence of non-study changes in the school environment that affect student nutrition and physical activity. Finally, data are collected to evaluate the degree to which the components of the intervention are delivered and administered as planned.

2 INTRODUCTION

In response to the dramatic increase in type 2 diabetes in the pediatric population, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) has sponsored a collaborative agreement, Studies to Treat Or Prevent Pediatric Type 2 Diabetes (STOPP-T2D), to develop and conduct both a treatment and prevention trial of type 2 diabetes (T2D) in children and adolescents. The prevention trial is the responsibility of the STOPP-T2D Prevention Study Group. The Prevention Study Group is composed of investigators from seven field centers (Baylor College of Medicine, Oregon Health & Science University, University of California at Irvine, University of North Carolina at Chapel Hill, Temple University, University of Pittsburgh, and University of Texas Health Science Center at San Antonio), the NIDDK project office, the coordinating center at George Washington University, the study chair, and other experts.

The prevention trial implements a population-based intervention to affect risk factors for type 2 diabetes in youth. The study group determined that middle school is an ideal environment for this intervention. Middle school children are typically undergoing pubertal changes that increase insulin resistance, alter body composition, and affect other risk factors for type 2 diabetes. Diet and physical activity behaviors are in flux during this period, and this transition represents an optimal opportunity to encourage healthier behaviors. Students this age are developmentally capable of increasing personal responsibility for behavior change and able to complete self-report assessments reliably.

The study group also determined that to impact risk for type 2 diabetes would require intervening on multiple levels, i.e., environmental, social, and individual. The environmental portion of the intervention changes the physical education class lesson plans and modifies the foods served in school. The behavior change intervention aims to enhance appropriate behavior choices within the school environment and extend positive lifestyle choices beyond the school environment. Social marketing and communication strategies reinforce diet and activity changes in and out of school. Finally, school staff and parents/guardians receive information and incentives to encourage them to help students adopt healthy lifestyles.

This protocol focuses on the design and organization of a primary prevention trial in 42 schools (6 per field center) randomized to a multi-component integrated intervention or to control. The primary purpose is to test whether the intervention has a significant impact on risk for T2D compared to control. School is the unit of sample size, randomization, intervention, and analysis, and data are collected at both the school and student level at baseline (beginning of 6th grade), across the administration of the intervention, and at end of study (end of 8th grade). All students in the school are exposed to the environmental changes and all students at the appropriate grade level are exposed to behavior change initiatives. Only students with appropriate parental consent and self assent participate in data collection.

The protocol was written by members of the Prevention Study Group, produced and distributed by the coordinating center, approved by the STOPP-T2D Data Safety Monitoring Board, and approved by the Institutional Review Boards (IRB) of each participating field center prior to the initiation of recruitment of schools. More detailed study procedures are presented in the manual of procedures (MOP).

3 OVERALL OBJECTIVES

3.1 Primary

The primary objective is to moderate risk for type 2 diabetes in middle school students. Modifiable risk factors are indicators of adiposity and glycemic dysregulation. The indicators are:

- Body mass index (BMI) ≥ 85th percentile, adjusted for gender and age. The 85th percentile is approximately equivalent to a BMI of 25 kg/m^2 in adults. A report from the American Diabetes Association [2000] noted that children and youth with type 2 diabetes were at or above the 85th percentile. In the OGTT Feasibility Study, 49% of subjects had BMI ≥ 85th percentile.
- Fasting glucose (mg/dL). The results of the OGTT Feasibility Study revealed a mean fasting plasma glucose value of 98.2 mg/dL (sd=8.5) in a cohort of 8th graders. Since progression to pre-diabetes and diabetes is associated with elevation of fasting glucose levels, population-wide reduction in glucose levels would indicate reduction in the risk of developing diabetes.
- Fasting insulin (μU/mL). Insulin resistance, assessed by fasting hyperinsulinism, is a prime defect in progression to type 2 diabetes. In the OGTT Feasibility Study, mean fasting insulin was 30.1 μU/mL (sd=19.1). Population-wide reduction in the mean fasting insulin level would indicate lessening of insulin resistance and diminished risk for the development of diabetes.

The risk of developing T2D begins early in life, and it is evident that to decrease the prevalence of T2D throughout the age spectrum, interventions to reduce risk factors should begin as early as possible. Middle school represents the ideal time since children progress through puberty, a period known to augment adiposity and insulin resistance. A BMI greater than the 85th percentile was associated with elevated fasting glucose and insulin levels in our pilot study [STOPP-T2D Prevention Study Group (in press)], and almost 50% of subjects were in that category. As a result, the trial has been powered to detect a difference in the percent of students with a BMI ≥ 85th percentile between the intervention and control schools at the end of 8th grade. In addition, differences in mean fasting glucose and insulin levels, as indicators of dysglycemia and insulin resistance, in intervention and control schools will be important outcome measures to assess if the intervention has reduced the risk for T2D.

3.2 Secondary

Major secondary objectives are to:

- Contribute to our understanding of the etiology of risk of T2D in this age group. In addition to comparison of intervention versus control, the control schools provide natural history data about the components of the metabolic syndrome (lipids, adiposity, blood pressure, fasting glucose), effect of family history, and pubertal status.
- Evaluate the ability of the intervention to influence lifestyle changes and choices both in and out of school:
  - Increase intake of dietary fiber, fruits, and vegetables and decrease intake of high fat and high sugar foods.
  - Increase intake of water and low fat milk and decrease intake of added sugar beverages.
  - Increase amount of physical activity and decrease amount of sedentary behavior.
- Determine the cost-effectiveness of the intervention.
- Monitor and describe the influence of changes in the school environment that are not mandated by the study but are due to decisions and changes in policies, guidelines, and recommendations at the school district, local, state, and national levels.

- Evaluate trends in academic performance, attendance, and comportment in intervention versus control schools.
- Evaluate the degree to which the components of the intervention are delivered and administered as planned, including the success of the school-wide communications campaigns to maximize study awareness, disseminate key intervention messages, and engage students.

4 BACKGROUND, SIGNIFICANCE, AND RATIONALE

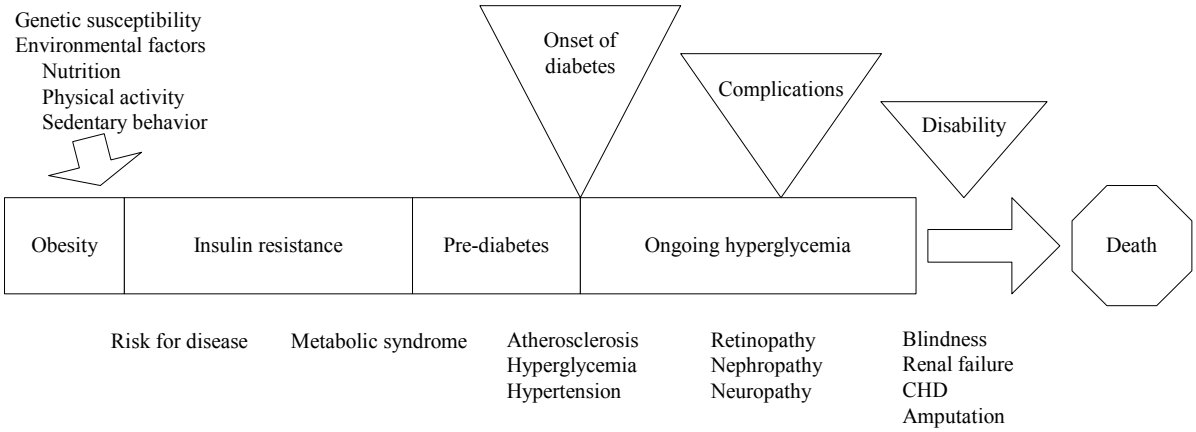
Type 2 diabetes has recently become increasingly more common in the pediatric and adolescent population. Prior to 1994, type 2 diabetes was unusual in the pediatric population; some clinics now report that up to one-third of children and youth presenting with diabetes between the ages of 10 and 19 years have type 2 diabetes [Dean et al. 1992; Pinhas-Hamiel et al. 1996; Rosenbloom et al. 1999; Scott et al. 1997]. Type 2 diabetes in youth, as in adults, is due to a combination of insulin resistance and relative beta cell failure, and is seen almost exclusively in those with excess adiposity. Insulin resistance is most often the first abnormality that develops due to an interplay between genetic factors and environmental triggers. Initially, insulin resistance is characterized by high circulating insulin levels; however, insulin levels decrease as beta cell dysfunction progresses, leading to frank diabetes [Nijpels 1998].

Once type 2 diabetes develops, most youth require treatment with glucose-lowering medications such as insulin, insulin secretogogues, insulin sensitizers, or agents that inhibit hepatic glucose release [Rosenbloom et al. 1999]. The contribution of lifestyle modification has not been studied in youth once frank diabetes is established. However, studies in adults suggest that modification of lifestyle and weight loss can decrease insulin resistance, improve measures of glycemic control, and reduce lipemia, and blood pressure [Hughes et al. 1984; Henry et al. 1986; Amatruda et al. 1988].

4.1 Pathophysiological Risks Related to T2D in Adolescents

Figure 1 summarizes the progressive development of type 2 diabetes, from influential factors to consequent symptoms, diagnoses, and sequelae.

Figure 1. Natural History of Type 2 Diabetes



4.1.1 Obesity

Obesity is a major risk factor for the insulin resistance that precedes the development of impaired glucose tolerance (pre-diabetes) and type 2 diabetes. Over the last decades, there has been a dramatic increase in overweight in youth; the proportion of youth aged 12-17 years with a body mass index (BMI) ≥ 85th percentile has increased from 15.2% (National Health and Nutrition Examination Survey, or NHANES II) in the 1970s to 25% (NHANES III) in the 1990s [Troiano and Flegal 1998]. Those at highest risk for being overweight are Hispanic, African American, and Native American youth and those with a positive family history of obesity—the same population of children at risk to develop type 2 diabetes. The vast majority of youth who are overweight will progress to obesity as adults and will have increased long-term morbidity and mortality [Harlan 1993; Mossberg 1989; Must et al. 1992]. As a result of the increasing epidemics of obesity and diabetes, obesity cost the nation more than $100 billion in 2002 [Allison, Fontaine, et al. 1999; Allison, Zannolli, et al. 1999; Visscher and Seidell 2001; Wolf and Colditz 1998] and diabetes cost $132 billion dollars. Indeed, the direct health care costs associated with obesity constitute 5.7% of the national health expenses in the US [Wolf and Colditz 1998] and those of diabetes almost 7% [ADA 2003].

Lifestyle factors, specifically, physical inactivity and poor dietary intake, are important targets for the primary prevention of obesity, insulin resistance, pre-diabetes, and type 2 diabetes. Controlled clinical trials have shown that type 2 diabetes can be prevented in adults with lifestyle interventions [Eriksson and Lindgarde 1991; Pan et al. 1997; Tuomilehto et al. 2001; DPP Research Group 2002]. While these studies were conducted in self-selected volunteers who were likely motivated to make lifestyle changes, there is reason to anticipate that youth might have a similar positive outcome to a comprehensive intervention combining diet and physical activity changes if they can be motivated to make the health-related lifestyle changes.

4.1.2 Influence of Diet and Activity on Insulin Resistance

Poor eating and drinking habits have been identified as risk factors for obesity [Kuller et al. 1995; Marstan and Stunkard 1980; Obarzanek et al. 1994]. Childhood obesity is associated with excessive consumption of sweetened beverages, fruit drinks, and fruit juices due to the kilocalories they contribute to the diet [Jacobson 1998; Levine 1997]. Soda machines can be found almost everywhere in the US, and the consumption of sugared soft drinks and fruit-flavored beverages by teens has more than doubled since 1965. The average adolescent boy now consumes 50 ounces of sugar-containing soft drinks and sugared fruit beverages per day [Popkin et al. 2001]. Data from the USDA Continuing Surveys of Food Intakes by Individuals (CSFII) from 1977 and 1995 indicated the proportion of adolescent boys and girls consuming soft drinks, the biggest source of refined sugar in the diet, increased by 74% and 65%, respectively [Keenan et al. 1996]. In addition, the current intake of fruit and vegetables by children is less than one-half of the recommended 5-a-day goal [Cullen et al. 1997; Domel et al. 1995].

It appears that a diet high in fruits, vegetables, and whole grain products, and low in total calories and dietary fat is likely protective against both obesity and type 2 diabetes. Several studies have found an inverse relationship between fruit/vegetable consumption and dietary fat intake [Kristal et al. 1990; Subar et al. 1994], suggesting that messages to eat more fruits and vegetables may have a beneficial effect on fat intake. Therefore, there are sufficient data to suggest that targeting youth to reduce calorie consumption in the form of sugar-containing sodas and juices and encouraging the intake of fruits, vegetables, and whole grain products should reduce obesity, insulin resistance, and the subsequent progression to diabetes.

Numerous investigations in adults show that physical inactivity promotes the development of obesity, insulin resistance [Andersen et al. 1998], pre-diabetes, and diabetes [Burchfiel et al. 1995; Dowse et al. 1991]. Conversely, exercise can improve glucose tolerance [Saltin et al. 1979] and insulin sensitivity [Ebeling et al. 1993; Henriksson 1995; Houmard et al. 1991; Ploug et al. 1990;

Ritenbaugh et al. 2003]. The effect of exercise on glucose tolerance and insulin sensitivity is multifaceted. There is a direct, short-term effect through activation and translocation of muscle GLUT-4 receptors, which improve cellular glucose uptake, independent of insulin [Holloszy and Narahara 1967; Houmard et al. 1991; Roberts et al. 1997]. Exercise also causes a decrease in circulating insulin levels [Wasserman 1995]. This effect is seen with short-term (10-30 minute) submaximal exercise, prolonged submaximal exercise (60-180 min), maximal-intensity exercise, and resistance exercises [Gyntelberg et al. 1977; Hartley et al. 1972; Lavoie et al. 1997; Miller et al. 1984; Viru 1992]. The mechanisms causing the exercise-induced decrease in insulin are not completely understood. It appears that exercise causes increased sympathetic activity, stimulating the alpha-adrenergic receptors of the pancreatic beta cells, which then decrease insulin secretion. This reduction appears to be sustained longer than the sympathetic response to exercise, well into the recovery phase after exercise (i.e., hours) [Mikines et al. 1988]. Aerobic exercise training results in lower resting insulin levels and improves insulin sensitivity [Winder et al. 1979]. Increases in insulin sensitivity and GLUT-4 transport protein content of the muscle occur in as little as 7 days of beginning exercise training [Etgen et al. 1997; Goodyear et al. 1990; Gulve and Spina 1995; Vukovich et al. 1996]. The improved sensitivity and transporter changes maximize after about 2 weeks of training; however, they last only 3 to 6 days after the cessation of training [LeBlanc et al. 1981; Vukovich et al. 1996]. This suggests the need for a continuous program of exercise to maintain insulin sensitivity.

Short-term studies of exercise training in youth also suggest a beneficial effect on insulin and glucose responses. Gutin et al. [1996] and Owens et al. [1999] evaluated a 10-week exercise and lifestyle program in 7-11 year old obese youth. No change in fasting insulin was found, but fasting glucose and glycohemoglobin levels declined. Kahle et al. [1996] found that a 15-week mild exercise program for 7 obese adolescents, which induced weight loss, resulted in improved insulin sensitivity and lowered resting plasma glucose values. In these studies, improvement in fasting glucose levels could have been related to either weight loss or exercise. McMurray et al. [2000] studied 362 African American and Caucasian youth 10-14 years of age. They found that 8 weeks of exercise training lowered resting insulin levels in only those youth who increased aerobic power, regardless of weight change. Recently, Ritenbaugh et al. [2003] implemented an activity and nutrition intervention with Zuni youth aged 16-18 years. The results failed to show a change in glucose but did show a decrement in fasting insulin levels. The results of these investigations suggest that an exercise program of sufficient duration and intensity should be able to influence the insulin sensitivity in youth.

4.2 Previous Interventions

4.2.1 Prevention of T2D

In adults, compelling evidence exists that type 2 diabetes can be prevented or delayed by lifestyle modifications aimed at weight reduction by improving nutrition and increasing physical activity. Collectively, these studies suggest that modest weight loss (in the range of 7–10 lbs), achieved through sustained lifestyle modifications, reduces the incidence of diabetes in high-risk individuals by 40–60%.

The Da Qing study [Pan et al. 1997] in China randomized 33 clinics (557 individuals with impaired glucose tolerance) to either control, diet, exercise, or combined diet plus exercise interventions. The incidence of diabetes was reduced in all three intervention groups (31%, 46%, and 42%, respectively) when compared with the control group. The Finnish Diabetes Prevention Study [Tuomilehto et al. 2001] was a 3-year study of 522 obese individuals with impaired glucose tolerance, randomized to either control or lifestyle groups. The lifestyle intervention had goals of a 5% weight loss, reduction in calories from fat, increased fiber intake, and moderate exercise of at least 30 minutes daily. The incidence of diabetes was reduced by 58% in the lifestyle group compared with

the control group. The lifestyle group had a net weight loss of 2.7 kg over the three years when compared with the control group.

While these studies involved subjects in other countries and relatively homogeneous study populations, the US Diabetes Prevention Program (DPP) demonstrated the efficacy of lifestyle intervention to prevent or delay type 2 diabetes in a culturally and ethnically heterogeneous population [DPP 2002]. In the DPP, more than 3000 adult subjects with impaired glucose tolerance were randomized to receive either placebo, metformin, or a lifestyle modification program. The goal of the lifestyle intervention was at least a 7% weight loss through a healthy, low-fat diet and at least 150 minutes of moderate physical activity per week. The study population was 19.9% African American, 15.7% Hispanic, and 5.3% American Indian. The lifestyle intervention reduced the incidence of diabetes by 58% over an average follow-up period of 2.8 years. Average net weight loss was 5.5 kg in the lifestyle group compared with the placebo group.

Given the recent nature of the rise of type 2 diabetes in the pediatric population, there have been no large scale studies with physiologic outcomes focused on diabetes prevention in youth. A recent study has suggested that population-based lifestyle interventions may ameliorate risk factors for type 2 diabetes in children. The Bienestar study randomized 27 elementary schools in San Antonio and provided a multi-faceted health program to Mexican American 4th graders [Treviño et al. 1998]. Mean fasting blood glucose was statistically lower in the intervention schools compared to the control schools (89.47 mg/dl v. 87.53 mg/dl).

The adult diabetes prevention studies focused on high risk subjects and generally included individuals motivated to make lifestyle changes. However, given the definitive results in the adult population, it is likely that a robust, comprehensive program targeting diet and physical activity changes would have a positive outcome in youth. Similarly, in adults there is ample evidence that lifestyle modification and weight loss can improve diabetes outcomes [Consensus Development Conference 1987; Franz et al. 2002; Wing 1995; Hensrud 2001]. These interventions in adults have been delivered in the clinical setting, but these findings suggest that comprehensive programs targeting youth, including those with type 2 diabetes, may have a positive effect on the course of diabetes in affected individuals.

4.2.2 School-based Efforts

Investigators have reported few interventions to prevent type 2 diabetes in youth. The only large randomized intervention study targeting prevention of type 2 diabetes was Bienestar (referred to in the previous section) which was designed to reduce diabetes risk factors in 4th grade Mexican American children through a comprehensive school health program [Treviño et al. 1998]. The study involved approximately 1400 youth from 27 elementary schools in Texas. At one year follow-up, intervention youth showed significantly lower fasting glucose than those in comparison schools. Adiposity did not differ between groups [Treviño et al. 1998; Treviño et al. 2004]. There have been several published pilot diabetes prevention programs. The Zuni Diabetes Prevention Program was a pilot intervention in two schools that involved diabetes education, a school-based wellness center, supportive social networks, and modification of the food types available to teens [Teufel and Ritenbaugh 1998; Ritenbaugh et al. 2003]. After 3 years there was a significant reduction in soft drink consumption and a decrease in fasting insulin levels, with no change in fasting glucose concentrations [Ritenbaugh et al. 2003]. Jump Into Action was a program designed for 5th graders living on the Texas-Mexico border [Holcomb et al. 1998]. The intervention consisted of a health education program designed to improve the knowledge, self-efficacy, and health behaviors of the participant children. Although the 1,114 children increased their health knowledge and self-efficacy for improving health behaviors, there was no change in exercise related behaviors. No physiologic variables were measured in this trial. The Quest program was developed to prevent type 2 diabetes in Pima children, but no outcomes have been reported [Cook and Hurley 1998].

Other school-based interventions with children and adolescents have targeted related outcomes such as obesity and CVD risk factors [Donnelly et al. 1996; Gortmaker et al. 1999; Marcus et al. 1987; Resnicow 1993; Resnicow and Robinson 1997; Simons-Morton et al. 1991; Stone et al. 1998; Tell and Vellar 1988]. School-based studies focused exclusively on obesity prevention include Planet Health [Gortmaker et al. 1999], Robinson's TV reduction intervention [Robinson 1999], PATHWAYS [Caballero et al. 2003], and others [Donnelly et al. 1996; James et al. 2004]. Most reported null findings on adiposity [Donnelly et al. 1996; Caballero et al. 2003; Resnicow 1993; Resnicow and Robinson 1997; Stone et al. 1998]. Exceptions include Planet Health, Robinson's TV reduction pilot study, and the UK "fizzy" beverage intervention [James et al. 2004]. The significant effects of Planet Health were generally limited to Black girls, whereas the effects of the UK "fizzy" beverage study were limited to students in the upper end of the BMI distribution. MSPAN (Middle School Physical Activity and Nutrition) showed an effect on adiposity in boys only [Sallis et al. 2003]. Of the studies that showed some positive effects on adiposity, it may be noteworthy that three had rather narrow foci, two focused on reducing television time [Gortmaker et al. 1999; Robinson 1999] and one on reducing sweetened beverages [James et al. 2004].

Some studies, such as the large Child and Adolescent Trial for Cardiovascular Health (CATCH) Trial [Luepker et al. 1996], the CHIC study [Harrell et al. 1999; McMurray et al. 2002], the Sports, Play, and Active Recreation for Kids (SPARK) Study [Sallis et al. 1997; Sarkin et al. 1996], and others [Burke et al. 1998; Donnelly et al. 1996; Keenan et al. 1996] were successful in increasing physical activity and the amount of time spent in school physical education (PE). CATCH also improved eating habits but had no impact on obesity rates or cholesterol levels. Of these studies, only the CHIC-I study was able to improve physiologic outcomes, i.e., to reduce body fat, to decrease cholesterol concentrations, and to increase aerobic power in elementary school children [Harrell et al. 1999]. The CHIC-II study was effective in reducing body fat and blood pressure in middle school youth [McMurray et al. 2002]. It is hypothesized that one of the main reasons the CHIC interventions were successful in affecting physiologic variables is the increased amount of time spent in actual moderate to vigorous physical activity (MVPA) in school (20 minutes in elementary schools and 30 minutes in middle schools).

4.3 Rationale for the Current Protocol

The rationale for conducting the primary prevention trial in youth in middle schools—and particularly targeting physical education class, total school food environment, and behaviors and messages—is as follows.

<u>In this age group</u>. Children in the 6th-8th grades (middle school) are generally 11-14 years old and in early adolescence. This is a time of both physical and metabolic as well as emotional and mental growth and development. Children are assuming more responsibility for their own choices. By developing a comprehensive intervention to alter the nutrition and physical activity practices of middle school children, excessive weight gain and obesity could be prevented or lessened. By preventing or lessening obesity, insulin resistance should be ameliorated and glucose intolerance (pre-diabetes) and diabetes prevented. In addition, established diabetes may be impacted by weight loss and improved physical activity.

<u>In schools</u>. The school environment can influence activity and eating habits [Skinner et al. 2000]. Richter et al. [2000] performed an extensive review of the environmental factors that relate to physical activity and nutrition in youth. They considered the key factors to be the number and type of exercise programs, exercise facilities, policies, types of health promotion activities, presence or absence of certain foods, ways in which food is displayed, and the presence of positive or negative consequences for physical activity and eating. In addition, teacher influences and role modeling and the social network affect the psychosocial culture and the social norms of the school. All of these

factors are considered to be part of the school climate, which can influence health behaviors of students, faculty, and staff [Cullen et al. 1999; Glanz et al. 1995; Paradis et al. 1995]. Barnett and Casper [2001] recently proposed a comprehensive definition of social environment as "the human social environment encompassing the physical surroundings, social relationships, and cultural milieus in which [children and adolescents] function and interact". The school is the primary social environment of youth, and as a result the school setting remains the predominant avenue in which to place interventions aimed at changing physical activity patterns in youth [King et al. 1995; Stone et al. 1998]. Policy recommendations and guidelines for increasing physical activity in youth include the school as an important environmental influence on physical activity [American Academy of Pediatrics 2000; National Center for Chronic Disease Prevention and Health Promotion 1997].

In addition, school based learning activities provide a knowledge base and rationale for change. Both retrospective and prospective research [Botvin et al. 1990; Gottfredson and Wilson 2003; Mellanby et al. 2000; Story et al. 2002; Goldberg et al. 1996a; Goldberg et al. 1996b; Goldberg et al. 2000; Elliot et al. 2004] demonstrates that well designed and implemented programs are effective in promoting a wide range of beneficial health behaviors among adolescents, including reduction in drug use, improvement in nutrition practices, and enhancing exercise self-efficacy. These benefits have been achieved by adolescent males and females, can be sustained beyond the intervention time period, and may be long lasting.

Many adolescent behaviors are shaped more by peers and social influences than by parental or other adult influences [Bandura 1977], and the school provides an environment conducive to fostering peer communications. Strong associations have been found between adolescents' actions and their peers' conduct through perceived normative behaviors and modeling [Backman et al. 2002]. For example, subjective normative use is a significant predictor of intention to drink regular soda [Kassem et al. 2004]. Furthermore, healthy and unhealthy behaviors often cluster among adolescents. The Youth Risk Behavior Surveillance System found significant relationships between sedentary lifestyle and unhealthy nutrition practices. For example, low physical activity among adolescents was associated with low fruit and vegetable consumption [Grunbaum et al. 2002]. Thus, focusing on enhancing one healthy behavior may positively impact other behaviors.

<u>In physical education class</u>. Adult studies report that exercise of at least 40% of maximal capacity performed for a minimum of 20 minutes results in a lowering of insulin levels [Bonen et al. 1985; Galbo et al. 1975; Hickson et al. 1979; Rubin 2001]. Other adult studies have shown that exercise training can have a positive impact on the glycemic status of normal individuals [LeBlanc et al. 1983; Mayer-Davis et al. 1998] and patients with type 2 diabetes [Ericksson et al. 1996; Larsen et al. 1999; Rice et al. 1999]. Similar studies on children present a less clear picture of the effects of exercise on glycemic status [Gutin et al. 1995; Kahle et al. 1996; McMurray et al. 2000; Schmitz et al. 2002]; however, the studies by Kahle et al. and McMurray et al. suggest that moderate intensity exercise for 8 to 15 weeks can result in improvement in the glycemic status, particularly in 'at risk' youth.

Data from CATCH [Leupker et al. 1996], which found no measurable physiological improvement in fitness, and others [McMurray et al. 2000; Rowland 1996; Eliakim et al. 1996] suggest that the amount of physical activity must lead to at least a 6% increase in total energy expenditure (TEE) over current levels before any change in fitness (VO_2max) occurs. Because any effect of exercise on insulin sensitivity lasts about 48-72 hours [Mikines et al. 1988], PE every other day is warranted. Using these data and assuming 3 PE classes per week and an overall resting metabolic rate for this aged adolescent of approximately 1.34 kcal/kg/min [Harrell et al. 2005], to achieve a 6% increase in TEE the adolescent should exercise for the equivalent of three 35-minute periods per week during which energy expenditure equals about 5.4 kcal/kg/min (less time is required as intensity increases). This translates approximately into three 35-minute periods in which the mean heart rate is 130-140 beats per minute. This amount of exercise in an unfit, overweight adolescent should result in a decrease in fasting insulin of approximately 10-50% based on the research by Kahle et al. [1996] and

Kang et al. [2002]. Furthermore, the heart range of 130-140 would be classified as at least moderate intensity [Harrell et al. 2005].

Eliakim et al. [2001] have shown that in children a 10% increase in energy expenditure is needed to increase aerobic power approximately 8%. Furthermore, to overcome the increased portion sizes requires approximately a 10-12% increase in energy expenditure [Rolls et al. 2004]. Taken together these results indicate that a minimum of 25 minutes of MVPA is needed in a PE class to cause the desired energy expenditure. Assuming PE classes meet 3 times a week, this amounts to approximately 75 minutes of MVPA per week.

In the total school food environment. Among older children and adolescents, energy intake, physical activity, and recreational inactivity are associated with changes in energy intake. In the Growing Up Today Study of over 10,000 children 9-14 years of age, a one-year rise in caloric intake predicted larger BMI increases (girls .0059 ± .0027 kg/m^2 per increase of 100 kcal/day; boys .0082 ± .0030) [Berkey et al. 2000]. In a 13 year longitudinal study of 243 children followed from ages 2-15 years, energy-adjusted fat and carbohydrate intakes were respectively directly and inversely related to skinfolds but not to BMI [Magarey et al. 2001]. Higher energy intake may be attributed to increased soft drink consumption, low-nutrient calorie-dense snacks, and absence of lower caloric, higher nutrient dense foods including fruit, vegetable, and grain based foods in children's diets. For each age and gender group of children between 2-19 years who participated in NHANES III, soft drinks contributed a higher proportion of energy for overweight than for non-overweight children and adolescents [Troiano et al. 2000]. A Canadian study of obese and non-obese children between 4-16 years of age reported that obese subjects consumed significantly more sugar (167 ± 60 g) than did the non-obese subjects (134 ± 46 g) [Gillis et al. 2002]. While there is no clear evidence that consumption of sugar per se affects food intake and weight gain, there is evidence to suggest that energy consumed as a liquid may be less well regulated than energy consumed in a solid form. Several studies suggest that consumption of soft drinks and other sweetened beverages is related to increased caloric intake [Troiano et al. 2000; Ludwig et al. 2001]. Of all the food groups, fruits and vegetables are most likely to be consumed in inadequate amounts by children. School-based interventions have been successful in increasing fruit and vegetable consumption, frequently with a concomitant decrease in fat intake [Lowe et al. 2004].

Parallel to the upward trend of children's body weight, a change of dietary intake has been observed. More children are snacking and there are increased intakes of added sugars and grain dishes high in fat as well as a decreased consumption of milk [Jahns et al. 2001; Cavadini et al. 2000]. In 1994-1996, 92.6% of children ages 6-11 years reported snacking on any given day, up from 76% in 1977. The number of snacks per day increased from 1.5 in 1977 to 2, and the amount of calories coming from snacks increased from 347 in 1977 to 462 in 1996 [Jahns et al. 2001]. When examining the types of food consumed as snacks, beverages (mainly soft drinks, fruit juices, and milk) are popular as well as savory-salt foods (potato chips, crackers, etc.) and high fat desserts. In addition, increases in portion sizes over the years have been observed. Data for Americans ages 2 years and older showed larger portion size consumption for both at home and away from home consumption [Nielsen and Popkin 2003].

Students participating in the National School Lunch Program (NSLP) are almost twice as likely to report eating vegetables at lunch (73% vs 40%) and consuming more fruit compared with non-participants (48% vs 32%), while students not eating NSLP meals were three times more likely to report consuming sweetened beverages, sweets, and sugar (64% vs 21%) compared with NSLP participants [Devaney et al. 1993]. When students transition to middle schools, they often gain access to snack bar and a la carte items in addition to NSLP meals [Devaney et al. 1993]. In middle schools, 88.5% of a la carte food items are high in fat and/or sugars [Wildey et al. 2000]. This environment does not foster healthful eating practices consistent with the Dietary Guidelines for Americans [Harnack et al. 2000].

In behaviors and messages. If childhood overweight and the associated risk factors are a consequence of biologic and social influences that operate across many settings, the development of effective public health interventions requires that strategies address multiple settings and multiple behaviors simultaneously [Dietz and Gortmaker 2001; Patrick et al. 2004]. Environmental changes to food offerings and physical education class have little resonance without the impact of behavior change, messages, and awareness regarding the themes of choice, strength, and balance.

Recent evidence has documented the importance of decreasing behaviors associated with negative health outcomes, especially sugar beverages [Berkey et al. 2004; Mrdjenovic and Levitsky 2003; Boynton-Jarrett et al. 2003] and sedentary behavior [Utter et al. 2003]. Pediatric obesity intervention studies have demonstrated that lifestyle activities (i.e., increasing overall activity in daily life), as compared to programmed activities (i.e., structured physical activities) are associated with positive long-term weight trajectories in school aged children [Epstein et al. 1994]. A school-based educational program [James et al. 2004] targeted decreases in soda consumption ('fizzy drinks') among 644 7-11 year olds in southwest England. The intervention was delivered in 1 hour sessions four times per year and aimed to decrease both regular and diet soda intake. Results showed that consumption of carbonated drinks decreased significantly in the intervention group compared to controls as measured by self-report.

There is stronger evidence that limiting sedentary behavior affects excess weight. A school based study of 192 3rd and 4th graders [Robinson 1999] was the first experimental study to demonstrate a direct association between decreases in sedentary behavior (television, videotape, video games) and decreases in adiposity in both girls and boys. The intervention consisted of 18 hours of education, self-monitoring, a 'TV turnoff' challenge, a 7 hour a week TV budget, peer advocacy for reduced media use, and newsletters to enlist parental support. Although overweight increased in both intervention and control groups, children in the intervention group had significant relative decreases in BMI, triceps skinfold thickness, waist circumference, and waist–to-hip ratio. A recent study [Roemmich et al. 2004] showed that 8-12 year olds who earned TV time based on the number of pedometer counts they were able to achieve had a significantly greater increase in physical activity than the control group on whom no TV restrictions were placed. The change in time spent watching television was directly related to the change in BMI.

5 STUDY DESIGN

The primary prevention trial is primarily focused on public health and therefore targets the public, as opposed to a clinical trial which targets the individual patient (e.g., the Diabetes Prevention Program, or DPP, which randomized at-risk adults to 3 treatment arms to prevent occurrence of type 2 diabetes). The public is clustered together in various units (e.g., the community, the workplace, the hospital, the school), and hence public health primary prevention trials are also known as cluster design trials. The cluster is the unit of sample size, randomization, intervention, and analysis.

This protocol presents a cluster design trial with middle school as the cluster. Schools are randomized to either intervention or control. All students throughout the school are exposed to the intervention, which becomes embedded in the school environment. Measurements and observations are made at the community, school, grade, and student levels. Student data are collected only from those providing appropriate informed consent and assent. Baseline data are collected at the beginning of the 6th grade (2006-2007 school year) and final outcome data are collected at the end of the 8th grade (2008-2009 school year). The primary objective is to reduce the risk associated with the development of type 2 diabetes in intervention compared to control schools. The primary analysis is based on a cohort of students with no reported diagnosis of diabetes followed from baseline (6th grade) through end of study (8th grade). A total of 42 schools are recruited, 21 randomized to intervention and 21 to control. Each field center enrolls 6 schools. Schools are randomized by end of July 2006—well before student recruitment—in order to accommodate the advanced timing of food service bids and purchase orders in schools assigned to intervention.

Throughout this protocol, the term 'semester' is used generically to signify a period of approximately 4 months designating the first or second half of the school year. While most schools operate under the semester schedule, some schools have segmented the school year into other time periods.

5.1 Eligibility

5.1.1 School

School eligibility criteria are:

- The student body is representative of the adolescent population at risk for type 2 diabetes, defined as either at least 50% minority (African American, Hispanic/Latino, and/or Native American) and/or greater than 50% eligible for free or reduced lunch.
- Annual student attrition from all causes is ≤ 25% (estimate determined from data provided by the school).
- Expected cohort size at end of study is at least 50 per school determined by applying 50% anticipated enrollment rate and annual school-wide attrition rate over 3 years.
- School authorities are willing to accept randomization of an individual school to intervention or control. If a school is assigned to the intervention program, this means that the school must arrange for the following if needed:
  - students attend PE class for a minimum of 225 minutes every 10 days over the course of the intervention,
  - PE class attendance is mandatory and continuous for the cohort, that is, 6th, 7th, and 8th graders in the intervention school years (with school specified medical exceptions in individual cases), and
  - the school has at least one play area that satisfies intervention requirements as determined by the field center staff..
- School authorities permit grade-wide collection of height, weight, gender, age, and race/ethnicity at baseline (1st semester of 6th grade).
- The school assists with mass mailings of study materials (e.g., information packets, newsletters) to homes either by providing the local field center with the names and addresses of parents or by identifying procedures to mail materials from the school. All postage and materials are paid for by the study.
- The school district possesses or obtains Federal Wide Assurance (FWA) to conduct research. Because of the increased level of involvement, the schools and their employees are considered 'agents' of the field centers and, therefore, each school must acquire FWA. This is typically acquired at the school district level.
- Appropriate school authorities agree to adhere to the protocol.

5.1.2 Students

The intervention is implemented school-wide in schools randomized to intervention, and all students are therefore exposed. Eligible students are enrolled in both intervention and control schools to participate in scheduled data collection and evaluation.

A <u>cohort</u> is enrolled at the start of 6th grade to participate in baseline (6th grade), interim (7th grade), and end of study (8th grade) data collection. Eligibility criteria at 6th grade enrollment are:

- The student is enrolled in 6th grade in fall 2006.
- The student is able to participate in the school's standard PE program.

- The student's parent/guardian has provided informed consent indicating understanding of the study and willingness for the child to participate in data collection and evaluation procedures.
- The student has provided informed assent indicating understanding of the study and willingness to participate in data collection and evaluation procedures.

An additional cross-sectional sample of students is enrolled to participate in end of study data collection. Eligibility criteria at 8th grade enrollment are:

- The student is enrolled in 8th grade in spring 2009.
- The student's parent/guardian has provided informed consent indicating understanding of the study and willingness for the child to participate in data collection and evaluation procedures.
- The student has provided informed assent indicating understanding of the study and willingness to participate in data collection and evaluation procedures.

5.2 Recruitment and Retention Strategies

Success of research trials often depends on effective recruitment and retention of study participants. In this trial, the 'study participants' refer to schools, students, their parents, and school officials, staff, and faculty. Recent studies of subject participation in community-based research clearly indicate that the traditional researcher-centered model of recruitment and retention is not sensitive to the participating communities and individual subjects [Levkoff and Sanchez 2003; Potvin et al. 2003]. Therefore innovative participant and community centered recruitment and retention strategies are needed.

5.2.1 Recruitment

Recruitment occurs on several levels: school district, school, staff/faculty, parent, and student. Strategies used address all levels [Harrington et al. 1997; Sexton et al. 2003].

At the community level, study investigators and staff:

- Form a school advisory board comprised of state or district level superintendent or key administrators from the Department of Education, powerful or visible parents (such as current or past PTA president), school principals, classroom and PE teachers, and food service director at district or state level.
- Meet with the board periodically to receive feedback and advice about study interventions and procedures.
- Share the advisory board deliberations across the study group to monitor and guide study progress.
- The advisory board is recommended but not required at all sites.

At the school district level, study investigators and staff:

- Identify, contact, and inform key individuals at the district level about the study. These key individuals include those with a vested interest in the study (food service director, physical education director, health educator, district school nurse, etc.).
- Make direct contact with the superintendent of the school district or the individual in the district who is responsible for research.
- Determine the necessary procedures required to obtain permission to contact principals and to acquire Federal Wide Assurance in the district.
- Keep the school district officials informed of all study activities, including schools contacted, list of schools agreeing to participate in the study, and a copy of the protocol, if appropriate.

At the school level, study investigators and staff:

- Contact and meet with school principals to provide an overview of the study and determine their interest in having their school participate in the study.
- Provide the principal with a written summary of the details of the study, including what the study requires from the school as well as benefits to the school, teachers, parents, and students. Get feedback from the principal about possible barriers that may be encountered in the school, and discuss ways to overcome these.
- Respect the tight schedule of the principals and other administrators. It may be helpful to approach principals during the summer months and other periods of lighter work load.
- At the discretion of the field center, a signed memo of understanding may be used to assure that the principal and/or assigned administrator fully understand and agree to all aspects of the study, including willingness to be assigned to control or intervention.
- Identify, establish, and maintain clear lines of communication with appropriate school administrators and staff.
- Involve school principals in selecting and recruiting teachers to implement intervention components.
- Identify a Health Action Team (HAT) of adult stakeholders, including administrators, staff, faculty, and parents, for the purpose of advising and assisting the study staff in the logistics, space, timing, etc. of the intervention. This involves meeting with the study staff at least 2-4 times per year for about 1 hour. Such a group may already exist in the school or may need to be modified or created. The actual name does not have to be HAT but is determined locally.
- Coordinate all study activities with the school calendar and class schedules.

At the school faculty and staff level, study investigators and staff:

- Meet with all teachers to explain the trial and solicit support.
- Develop materials that explain the purpose of the study and provide a summary of data collection (suitable for both intervention and control schools) and that describe the intervention (for intervention schools only).
- Clearly define expectations of school staff and faculty and the roles and responsibilities of study staff.

At the parent and student level, study investigators and staff:

- Include in the consent packet a letter to parents from the field center principal investigator and the school principal indicating support and encouraging participation in the study.
- Provide materials at the appropriate reading level and in Spanish where needed.
- Hold parent meetings, orientation sessions, and/or registration opportunities to present materials and informed consent.
- Make student presentations and contacts to generate positive word of mouth.
- Use materials with the study logo to generate student interest in participating in the study.

5.2.2 Retention

Retention of schools and students is vital for a longitudinal cohort study. As with recruitment, retention addresses all levels of participant.

At the parent and student level, study investigators and staff:

- Provide written feedback to all parents of participating students about the results of the "health screenings" (i.e., measures from the pre and post intervention testing, see the section on Safety Monitoring and Reporting).

- Maintain interest in the study through materials and mailings for subjects in intervention schools.
- Send letters to parents and students prior to the final data collection, reminding them of the upcoming data collection and the incentives the students will receive.

At the school level, study investigators and staff:

- Provide periodic communications via newsletters and presentations to inform the school officials/staff, students, and parents about type 2 diabetes, the current status of the study, and plans for the next phase, as well as to acknowledge their support.
- Use experienced study staff who understand and respect local culture and customs.
- Become a presence in the intervention schools to monitor and maintain consistency in implementation, and to provide encouragement and trouble-shooting as needed. Within protocol parameters, be as flexible as possible with study schedule and proactive in resolving conflicts with schools.
- Provide school administration and faculty with the schedule or grid showing how the intervention fits into the school calendar with regard to testing, holidays, and other events.
- Solicit support from parents, school officials/staff, and teachers who can encourage students to participate in the intervention activities.
- Provide periodic incentives for school staff and teachers.
- Provide monetary incentives for the schools that increase with each year of the study. For control schools these are $2,000 for year 1, $4,000 for year 2, and $6,000 for year 3. For intervention schools, the amounts are $2,000 for year 1, $3,000 for year 2, and $4,000 for year 3.

5.3 Informed Consent and Assent

Each field center is responsible for obtaining IRB approval and informed consent and assent.

- School Staff and Employees. By acquiring Federal Wide Assurance (FWA) to conduct federally funded research, the school and its staff and employees are considered 'agents' of the field centers and informed consent is not needed for them to participate in implementation of the intervention, including training. Informed consent is required if school staff and employees are themselves the subjects of the research. Therefore, affected school staff and employees sign appropriate informed consent before being asked to provide survey, interview, or other evaluation data.

- Health Action Team (HAT). Each intervention school establishes a Health Action Team (HAT) to serve as an advisory body to the study staff. Such a group may already exist or may be created. Members of the HAT include school personnel as well as parents. No data are collected from the HAT members themselves, although meetings and attendance are tracked for process evaluation purposes. Local IRB guidelines apply to whether these individuals qualify for exemption or whether consent/assent need to be acquired.

- Students and Parents. Parental consent and student assent are obtained for data collection measurements and evaluation procedures, not for exposure to the intervention which is delivered school wide. For students enrolled in the 6th grade cohort, consent/assent covers data collection and evaluation procedures in 6th, 7th, and 8th grades. For students enrolled in 8th grade, consent/assent covers data collection and evaluation procedures in 8th grade (end of study).

Consent includes permission for the study group to draw and store an extra 10 mL (about 2 teaspoons) of blood to look for other possible diabetes and obesity related complications and risk factors. These measures do not have immediate clinical relevance, but may prove helpful in understanding and interpreting study results. In addition, future research may uncover new blood tests that would prove valuable to diabetes and obesity research in this age group. Therefore, the informed consent form includes a check box asking parents to give permission to eventually send all data collected for the study (including leftover blood samples), appropriately anonymized and de-identified, to be stored in the central NIH repository for use in approved research related to diabetes and obesity.

At each field center, consent is obtained from parents to provide information useful for the family outreach events and activities, including first-person stories for the newsletters. Up to two focus groups are conducted with parents per year, with 6-10 participants per focus group. Specifically, the need for a second focus group depends on the quality of the information obtained in the first round study-wide. Strategies for recruitment may include solicitation by mailed flyer or newsletter announcement, talking to the parent HAT member to recruit other parents, or through the school's community liaison or other school-based group with links to parents.

- Student Peer Communicators. In intervention schools, students are nominated by their classmates to participate as peer communicators. Students are given the opportunity to accept or decline the nomination. Students nominated to be peer communicators may or may not have provided consent and assent to be a study participant, and students who are willing to participate as peer communicators are not required to be members of the cohort providing consent/assent for scheduled data collection measurements and evaluation procedures. Students designated as student peer communicators are those who agree to serve as a student peer communicator, who are nominated by their classmates, and who are approved by the classroom teacher and/or school administration. Students selected to serve as peer communicators (1) attend 1-2 training sessions, (2) attend activity-specific refresher sessions, (3) assist study staff with selected intervention activities, and (4) as feasible in the school context, participate in informal small group discussions to inform study staff about design components for activities held during subsequent intervention phases. Peer communicator activities take no more than an average of 1 hour per week to perform during the active intervention phases of the study. Local IRB guidelines apply to whether these individuals qualify for exemption or whether consent/assent need to be acquired.

All participants may refuse to provide specific responses or measures or may withdraw from data collection procedures entirely at any time. All students and, to a lesser extent, all school staff are exposed to the intervention delivered throughout the school and in the classrooms. Under these conditions, withdrawal from the intervention may not be entirely possible. Parents who want to withdraw their child from any aspect of the intervention follow established school procedures.

5.4 Participant Compensation

Table 1 lists compensation items and amounts provided by the study. This list does not include study supplies, which are needed to deliver and implement the intervention or data collection activities, or small items given away to students, families, and staff school-wide or grade-wide to promote campaigns and activities.

Table 1. Study Provided Compensation		
Who	**What**	**Amount**
SCHOOL		
Intervention School	• school program enhancement • PE class equipment required to implement intervention • food service department to defray costs of nutrition intervention	• $2000 in year 1, $3000 in year 2, $4000 in year 3 • ~ $15,000 over 3 years • $3000/year
Control School	• school program enhancement	• $2000 in year 1, $4000 in year 2, $6000 in year 3
INTERVENTION SCHOOL FACULTY		
Classroom Teacher Delivering Intervention	• participation in 4-hour initial behavior intervention training • participation in 1-hour booster behavior intervention training • participation in data collection and documented delivery of intervention	• hourly rate ~ $25/hour once a year in 1st semester • hourly rate ~ $25/hour once a year in 2nd semester • $100/semester
PE Teacher	• participation in 6-hour initial PE intervention training • participation in 6-hour booster PE intervention training • participation in data collection and documentation of PE intervention	• hourly rate ~ $25/hour to teacher if occurs on teacher 'personal time', or to school to reimburse for substitute teacher during school calendar, once a year in 1st semester • hourly rate ~ $25/hour to teacher if occurs on teacher 'personal time', or to school to reimburse for substitute teacher during school calendar, once a year in 2nd semester • $100/semester
INTERVENTION SCHOOL STAFF		
FS Manager	• participation in 4-6 hour initial nutrition intervention training • participation in 2 hour booster training • participation in data collection and documented delivery of intervention	• $50 • $25/semester • $100/semester
FS Worker	• participation in 4-6 hour initial nutrition intervention training • participation in 2 hour booster training	• $50 • $25/semester
CONTROL SCHOOL STAFF		
FS Manager	• participation in 2-hour study procedures orientation	• $25/year

Table 1. Study Provided Compensation		
Who	**What**	**Amount**
FS Worker	• participation in 2-hour study procedures orientation	• $25/year
STUDENT		
All	• return consent form (signed or not) • participation in health screening data collection measures and forms	• gift item worth ~ $5 • $50 baseline (6th grade), $10 interim (7th grade), $60 end of study (8th grade)
FAMILY		
Intervention Parents	• focus groups to provide input about family outreach events and activities	• $35/year per parent, up to 2 focus groups per field center, 6-10 participants per focus group

5.5 Privacy and Confidentiality

Policies and procedures established in previous Prevention Study Group protocols are continued:

- Participants must provide appropriate informed consent and assent.
- All data entered and transferred to the coordinating center for accumulation in the central database identify the individual only with a study ID number. The coordinating center does not receive any personal identifiers.
- Each field center maintains a file on each individual that includes personal identifiers, including contact information, and links the individual to the study ID. These data are not entered into the study data management system. The files are kept in secure locations and the field center is responsible for taking every other reasonable measure (those set by the state, the site, and the study) to ensure and maintain record confidentiality and patient privacy.
- All study staff receive training on maintaining the privacy and confidentiality of individual information as well as cumulative study data. Procedures are implemented to protect an individual's privacy, e.g., use of screens in collection of physical measures.
- All study staff sign an annual letter agreeing to maintain privacy and confidentiality of individual data as well as emerging results.

5.6 Treatment Arms

5.6.1 Intervention

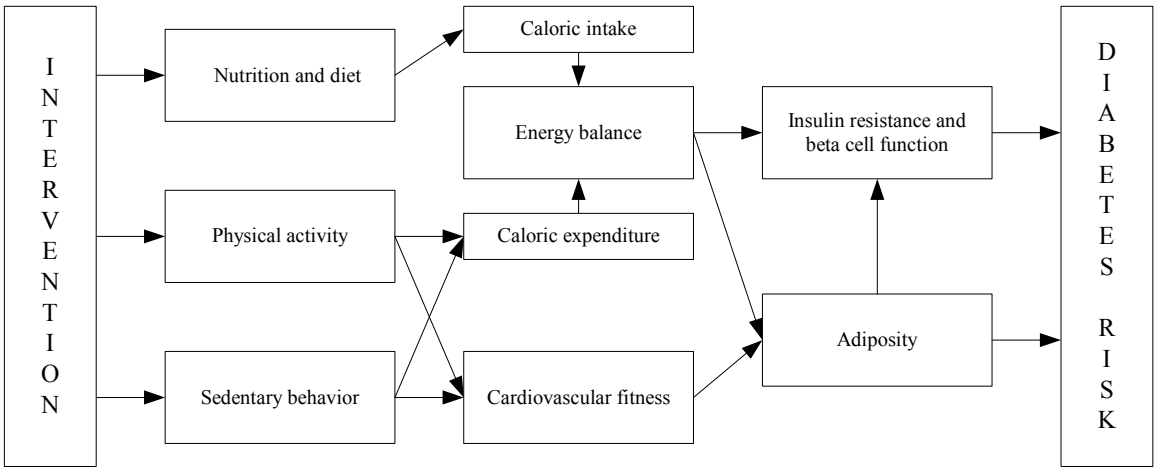
The intervention begins with fundamental changes to what is offered and delivered in the total school food environment and physical education classes, enhanced by a phased roll-out of messages and activities across grades to promote education and behavior change both in and out of school. The intervention consists of the following integrated components:

- changes in the nutritional quality of food and beverage offerings throughout the total school food environment, including cafeteria meals and after school snacks offered through federal programs such as the National School Lunch Program (NSLP) and School Breakfast Program (SBP), a la carte, and vending machines;
- changes in the physical education (PE) program and equipment to increase both participation and number of minutes spent in moderate-to-vigorous physical activity when implemented by PE teachers as part of classroom lesson plans;

- brief classroom activities designed to increase knowledge, enhance decision making skills, promote peer involvement and interaction, and enhance social influence;
- individual and group behavior change initiatives aimed at promoting healthier behaviors through self monitoring, goal setting, and problem solving;
- family outreach to involve parents/guardians and family members by providing information and strategies to support youth in accomplishing behavioral goals;
- school-wide communications to enhance and promote changes in nutrition, activity, and behavior.

Figure 2 shows the relationship between the intervention and the primary outcome.

Figure 2. Relationship Between Intervention and Diabetes Risk
(direction of relationship '+' or '–' not specified)



All intervention components are integrated in the delivery of a series of themes targeting specific behaviors and building upon each other. The phased roll-out of messages and activities keeps the program fresh and relevant. Activities are synced to specific school calendars and schedules. Table 2 gives the primary themes by semester, along with specific targeted behaviors:

- The <u>themes</u> highlight the overarching emphasis of promotional and educational campaigns and activities. Activity and nutrition are initially delivered as separate themes and then integrated into the theme of energy balance. In the second half of the 8th grade school year, a wrap-up campaign consolidates the messages of the previous semesters into the theme of "Strength, Balance, and Choice for Life". Students receive feedback on their health status by participating in the end of study health screening.

- The <u>targeted behaviors</u> ensure consistent delivery and reinforcement of messages addressing healthy lifestyle behaviors and changes. Nutrition and activity are continuously targeted. Behaviors become sequentially more complex, starting with education and knowledge based activities and extending to self monitoring, goal setting, and problem solving.

Table 2. Intervention Themes and Targeted Behaviors	
A. THEMES	
Second Half of 6th Grade	Water versus Added Sugar Beverages
First Half of 7th Grade	Physical Activity versus Sedentary Behavior
Second Half of 7th Grade	High Quality versus Low Quality Food
First Half of 8th Grade	Energy Balance: Energy In/Energy Out
Second Half of 8th Grade	Strength, Balance, and Choice for Life
B. TARGETED BEHAVIORS	
• Increasing water consumption	
• Substituting water for added sugar beverages	
• Drinking water for health, nutrition, and hydration	
• Choosing healthier foods and drinks for meals and snacks	
• Substituting nutrient dense, lower caloric foods for low nutrient, higher caloric foods	
• Self-monitoring, goal setting, and problem solving to increase intake of water, fruits, and vegetables	
• Increasing movement and accumulation of time spent being active	
• Decreasing time spent in sedentary behavior	
• Substituting physical activity for sedentary behavior	
• Self-monitoring, goal setting, and problem solving to increase physical activity and decrease sedentary behavior	

The intervention is accomplished by a two-pronged approach. First is a core of developed programs, materials, lesson plans, workbooks and manuals—i.e., the vehicles. Second is their implementation and delivery using various activities and strategies, including initial and booster training, one-on-one contact and strategic planning between school staff and study staff, and promotional educational and awareness events and campaigns. In order to conduct an efficacy trial that delivers the intervention with the greatest dose, fidelity, and reach, process evaluation data are collected and reviewed on an interim basis. Results are used to modify implementation and delivery in order to maintain the potency of the intervention and assure equal dose delivery and fidelity across sites.

5.6.2 Control

Control school activities emphasize recruitment and data collection. No 'placebo' intervention is delivered. Activities and efforts to retain the involvement of control schools and students throughout the trial are described in the section on Recruitment and Retention Strategies. As for intervention schools, parents receive a health screening report of the child's physical and laboratory measures at baseline and end of study data collection.

At the end of the study, control schools are offered a set of intervention materials (excluding equipment and training sessions).

6 INTEGRATED INTERVENTION COMPONENTS

The intervention components affecting physical education, total school food environment, behavior, and communications are integrated to deliver the phased roll-out of messages and activities according to the themes and targeted behaviors presented in Table 2. Each intervention component is described.

6.1 Physical Education Intervention

The PE Intervention Committee, in collaboration with experienced teachers and national experts, developed a PE class program of lesson plans in units or themes plus a training program that focuses on effective class management, reducing inactivity, and motivational techniques to maximize PE teacher willingness to participate in the intervention. The program was developed in a series of pilot studies and evaluated for performance (i.e., delivery of MVPA).

6.1.1 Overview of Goals and Strategies

The intervention focuses on increasing the moderate-to-vigorous physical activity (MVPA) levels in the physical education class. The PE intervention target is at least 150 minutes of MVPA over 2 weeks achieved in the required minimum of 225 minutes total PE class time every 2 weeks. The physical education class intervention has been developed with many activities that can be used to enhance MVPA, many administrative techniques that can be used to reduce inactivity during class time, and a training program that focuses on effective class management, reducing inactivity, and motivational techniques.

The intervention optimizes individual achievement so that children can attach values to their own improvements and can, therefore, appreciate improvement in their own skills and abilities. The program emphasizes the ability of PE teachers to choose from a variety of physical activities (individual and team oriented, aerobic, resistance training, and skill activities) that are faithful to state mandated policies governing public school physical education at the seven field centers and meet the study goal of increased MVPA.

The intervention is implemented and managed by the PE teacher in the classroom. The study staff physical activity coordinators (PAC) hired by each field center provide guidance. The PAC is responsible for conducting training sessions for the local participating PE teachers, and for maintaining a collaborative relationship with each teacher throughout the intervention to continue assisting with planning and trouble-shooting. In addition, the study provides each school with one PE teacher assistant to work with the PE teacher in class conducting the study provided units and lesson plans. The study also provides equipment needed to implement the intervention (worth about $15,000 per school over three years).

The intervention was developed to provide PE teachers with flexibility in teaching the units and lessons. The intervention consists of a core program for each grade level plus a set of choices. The core program consists of the following units/themes: basketball, fitness (6th grade only), soccer, team handball, and FLOW (Fitness Laboratory on Wheels). FLOW is a multi-station exercise program to increase cardiovascular fitness, strength, agility, and muscular endurance developed by a California PE teacher. FLOW gives the students a chance for personal achievement and includes fun activities. FLOW was well-accepted and enjoyed by most students in the previous pilot studies. The other four activity units have been previously evaluated in pilot studies and delivered MVPA for about 75% of the class period. Each core unit contains 10-12 lessons developmentally appropriate for 6th-8th grades. The core units are designed to increase in skill and fitness demands as the intervention progresses.

In addition to these four core units, the PE teacher can choose from the following units to complete the physical education program: cooperative games, dance, fitness, frisbee, football,

lacrosse, softball, street hockey, track and field, racket sports (badminton, pickleball, tennis, table tennis), swimming, and volleyball. These lessons focus on activities that keep all students involved, are designed to increase MVPA, reduce inactive time during the class, and teach skills or techniques required by state mandated curricula.

Finally, each site has the option to develop a unit/theme plan based on local customs and interests. For example, an area with a predominance of Native Americans may have games and activities relating to their heritage that could provide MVPA. These units are developed in consultation between the field center physical activity coordinators and the local PE teachers to ensure the rigor of the specialized unit, and are reviewed by other study group experts.

6.1.2 Schedule and Delivery

The physical education intervention is delivered over a two and a half year period to all students taking PE classes in 6th grade spring semester (2007), in 7th grade (school year 2007-2008), and in 8th grade (school year 2008-2009). In schools assigned to the intervention, all students in these PE classes participate in the study intervention. If the classes at the school are mixed by grade, then all those containing 6th graders initially receive the intervention. During the second and third years, all classes that contain 7th and 8th graders, respectively, receive the intervention.

Any physical education intervention needs to be concerned with growth and development that occur from 6th through 8th grades. This critical growth period from late childhood into adolescence is marked by the beginning of substantial changes in body structure and physiological development. There is the progression from fundamental movements to intermediate levels of motor skill performance connected to sport activities [Robertson 1984]. The quantitative performance changes seem to correspond to neuromuscular development and physiological growth [Seefeldt and Haubenstricker 1982]. Structural factors that provide a mechanical advantage become apparent and begin to influence the production of leverage and rotation needed to powerfully propel objects in running, jumping, throwing, kicking, and striking [Adrian and Cooper 1995]. The capacity to integrate perception of moving objects and initiate a motor response (e.g., hand or foot and eye coordination timing), for striking, kicking, and catching becomes stabilized about this time period [Gabbard 2004]. Practice and instruction in the basic movement skills and in combinations of these skills leads to physiologic and motoric changes. This strongly suggests that the PE curriculum needs to be adjusted by grade level to accommodate changing motoric capacities. The study intervention lesson plans increase motor skill complexity grade by grade within each unit. By increasing motoric capacities and improving fitness, the student attains an increased ability to exercise, resulting in improved self-concept and better enjoyment of exercise. Thus, the student is more willing to participate in future exercise programs. In addition, the increased complexity challenges the student to improve within his/her own capacity, and allows students to participate and experience new skills and a variety of physical activities.

Each field center study staff includes a physical activity coordinator (PAC) to oversee intervention implementation. In addition, the study provides a PE teacher assistant for each intervention school. Local PE teachers attend study conducted training sessions that focus on performing the units/lessons, effective management techniques to reduce inactive time during PE class, and ways to motivate youngsters. Regular consultation between the physical activity coordinator and local PE teachers continues to ensure the integrity of the intervention throughout the duration of the trial.

Success of the program is linked to each local PE teacher's willingness, motivation, and cooperation in delivering the intervention. A first step is to develop a professional and respectful relationship between the PE teacher and the physical activity coordinator, with the goal being to empower the PE teacher to actively engage in and implement the physical education intervention. This begins in initial meetings, in-class observation, and training, and continues in booster training and one-on-one sessions throughout the intervention.

6.2 Nutrition/Food Environment Intervention

The nutrition intervention component was developed by the Nutrition Intervention Committee, and focuses on 5 specific goals representing targeted changes in the foods served or offered to students in the total school food environment. Served refers to items taken by the student, either through sale or subsidized program; offered refers to all food and beverage items made available to students from which they may select. The total school food service environment comprises: the federal meal programs (National School Lunch Program or NSLP, the School Breakfast Program or SBP, the after-school snack program, and the supper program), a la carte (including snack bars and school stores), vending machines, fundraisers, and classroom parties and celebrations. Emphasis is placed on positive changes in foods and nutrients that improve student dietary intake. The main objective of the nutrition intervention is for schools to achieve and maintain all prescribed goals for the duration of the trial.

Outcome data measure (1) the specific changes to the school food environment in terms of what foods and beverages are served, how food is prepared, and consequent changes and trends in food and beverage purchases and (2) student dietary intake, especially changes in nutrients (total energy, percent energy from fat, snacks and desserts), food groups (fruits, vegetables, and whole grains), and beverages. The success of the intervention is dependent upon changing the total school food environment to serve and offer foods and beverages that are representative of choices that decrease intakes of added sugar beverages and low nutrient dense foods, while encouraging recommended intakes of fruit, vegetables, low fat food items, and whole grain or high fiber grain-based foods and legumes. The intervention is designed primarily to accomplish school food service environmental changes. Integrated activities with the behavior and communications intervention elements seek to move indicators of nutrient intake.

6.2.1 Overview of Goals and Strategies

The nutrition/food environment intervention component is designed to instigate early entry into the food purchasing process, leading to early and sustainable changes in foods/beverages served and offered. Periodic training and contact with school food service personnel and district staff are performed to maintain consistency of the intervention implementation as well as attention to and enthusiasm for making the change goals. Strategies are developed to address implementation approaches for each goal. Implementation and maintenance of successful changes are helped by consistent and sustainable interaction between the study staff research dietitian and the food service staff.

Changes to eliminate sweetened beverages available from vending beverage machines are recognized as a special challenge if ‘pouring contracts’ exist. This means that vending machine operations are not under the total control of the food service or school administration. The study makes aggressive efforts to implement goals targeting added sugar beverages in vending, starting with decreases and substitutions in 6th grade and complete elimination in 7th and 8th grades. These efforts include contact and arrangements with local and national sweetened beverage producers and distributors. Only schools that agree to comply with all aspects of the protocol including elimination of added sugar beverages in vending machines are eligible to participate in the study.

Total school food environment change goals are described in Table 3. These goals are based on the minimum number of food group servings that can be offered as part of the USDA school lunch/breakfast program and the maximum for which school food service currently receives reimbursement. Exceeding the minimum allowable servings is an additional cost factor.

Table 3. Nutrition/Food Environment Intervention Goals
Goal I: Lower the average fat content of food served in school.
Goal II: Serve at least 2 servings of fruit and/or vegetables per student on NSLP and at least 1 serving per student on SBP each day
Goal III: Serve all dessert and snack foods with ≤ 200 calories per single size serving and/or package.
Goal IV: Eliminate milk > 1%, all other added sugar beverages, and 100% fruit juice (100% fruit juice may only be served as ≤ 6 ounces as part of SBP and/or after school snacks).
Goal V: Serve at least 2 servings of grain-based foods and/or legumes (≥ 2 g fiber per serving) per student on NSLP and at least 1 serving per student on SBP each day.

The study investigators recognize that schools across the country are currently making voluntary changes to total school food environment offerings, motivated in large part by increased publicity and awareness of adolescent dietary intake and obesity levels. Therefore, goals and outcome strategies included in the intervention are relevant for each study intervention school, but there may be differences in implementation times. That is, some schools may have already implemented some aspects of the intervention and may have attained the goal at baseline but may need to focus on sustainability of those goals.

6.2.2 Schedule and Delivery

To implement the intervention, the field center study staff includes a research dietitian (RD) with experience and education in dietetics or nutrition and food service management. The RD works with the school food service staff to guide goal progress and achievement over time.

Targeted activities are sequenced to strengthen the focus and sustainability of the intervention:

- The RD participates in the recruitment of schools with attention to assessment of the current total school food environment at both the school district and local school level, including what foods and beverages are offered, how foods/beverages are purchased and prepared, how operations document production activities, and to review the food environment goals. The RD encourages food purchases and bids within schools randomized to intervention to support availability of alternative food/beverage products aligned with the intended goals.
- Pre-intervention, the RD implements training programs for all food service personnel at intervention schools. The RD works with the school managers to schedule and deliver a training workshop for the school food service staff prior to intervention implementation. Training includes an overview of type 2 diabetes in youth, a discussion of the relationship between diabetes and the obesity epidemic in this country, and an explanation of the prevention trial. Specific intervention objectives are explained for the school food service staff operational activities. These include the positioning of acceptable food and beverage items, 'best' food preparation and presentation practices, promotion ideas, and pricing issues. The food service staff learns about procedures and forms used to collect data needed to evaluate the outcomes. Refresher workshops are scheduled twice a year.
- In 6th grade RDs work with the food service staff to provide training and guidance in implementing the intervention environmental changes to support campaigns to introduce changes. A minimum number of outcome strategies are activated to achieve the nutrition goals. The cafeteria venue serves as an extended classroom. Activities targeting more water

and less added sugar beverages, awareness of broader benefits of a variety of new food choices, and the synergy between physical activity and food choices are introduced.

- In 7th grade activities to support achievement of all nutrition goals are continued. Support of concepts introduced in 6th grade is further enhanced by highlighting the role of lower fat and sugar snacks in the activities and messaging. RDs provide on-going training and guidance to food service personnel to sustain changes in food/beverages served as described in the goal statements. School campus vending issues are specifically targeted to increase access to more water and to healthy snack options. RDs participate in outreach to parents and educators designed to explain and expand the food and nutrition messages within the trial.
- In 8th grade continued support of goals and strategies introduced in 6th and 7th grades are further enhanced by highlighting the synergy between student dietary intake goals and the activities and messaging within the trial. RDs provide guidance to food service personnel to sustain the training introduced in the trial and to continue to make changes in food/beverages served as described in the goal statements. RDs participate in outreach to parents and educators designed to explain and expand the food and nutrition messages within the trial.

6.3 Behavior Intervention

The behavior intervention component was developed by the Behavior Intervention Committee to extend changes introduced in the school environment more broadly into affecting lifestyle choices both in and out of school. The behavior change intervention elements have been carefully selected to complement the other intervention components and include brief classroom activities, individual and group behavior change initiatives, and parent/family outreach.

6.3.1 Overview of Goals and Strategies

The behavior intervention is a combination of integrated components:

- FLASH (Fun Learning Activities for Student Health) are brief classroom activities designed to increase knowledge, enhance decision making skills, promote peer involvement and interaction, and enhance social influence.
- Self-monitoring campaigns are individual and group behavior change initiatives integrated into the FLASH activities that aim to promote healthier behaviors through self monitoring, goal setting, and problem solving.
- Family outreach activities involve parents/guardians and family members by providing information, strategies, and opportunities to support youth in accomplishing behavioral goals.

Each component incorporates communications strategies to maximize the attractiveness of the healthier behaviors and decrease the attractiveness of less healthy choices. Student peer communicators are identified to help in the implementation of the behavior intervention. In addition, within-site intervention challenges and sharing are extended throughout the intervention period to cross-site (study-wide) opportunities as feasible.

The behavior intervention components incorporate various behavior modification strategies:

- self monitoring;
- goal setting, emphasizing the concept of personal choice and self efficacy, and providing a knowledge base designed to motivate healthier choices;
- group competition, designed to build momentum over the weeks of the campaign; and
- reinforcement through social recognition and rewards.

Goal setting and self-monitoring occur throughout to reinforce and encourage children to ‘overlearn’ key skills that are essential for behavior change. Each semester’s activities refer back to prior goal-setting and self-monitoring activities so as to reinforce these skills and foster repeated practice of

these activities. Events and activities build upon each other. Targeted behaviors are reinforced by special recognition activities and items for participating in challenges and competitions.

6.3.2 Schedule and Delivery

6.3.2.1 In-class Activities: Fun Learning Activities for Student Health (FLASH)

FLASH (Fun Learning Activities for Student Health) is the term used to denote brief classroom modules used as a vehicle to promote nutrition and physical activity comprehension, enhance program synergy, and overcome barriers to healthy nutrition and physical activity practices. Each module is delivered in a series of activities within the classroom setting. Each activity is designed to last no more than 30 minutes. The planned content begins with the second half of 6th grade and continues to end of study. The activities target different aspects of nutrition and physical activity to correspond with the integrated intervention, as presented in Table 2.

The school principal and authorities responsible for scheduling choose the classes for FLASH activities. The selection and sequencing of the activities are pre-determined and provided in teacher manuals and student workbooks. Students work singly and in teams. Each of the activities in the module is self-contained, with a scripted introduction and conclusion. Elements are introduced to assist students in gaining knowledge and providing healthy peer influences. The activities begin with self-assessment to establish a baseline, and involve problem solving and scripted discussion points promoting maximum participation from all students, with each student involved in both thinking and doing. Application of cooperative skills, such as listening and communicating, problem solving, decision making, and sharing, allows for staged classroom control, with practice working together. Students begin to gain insight from each other as they complete a task related to better understanding of the health behavior. Small group work sharing and presentation are planned during the last activity of each module. Students also complete a brief self-assessment questionnaire as part of the final activity. Opportunities to share student-created messages across sites further enhances the importance of the study goals and builds enthusiasm for behavior change.

6.3.2.2 Behavior Change Initiatives: Self-monitoring Campaigns

The self-monitoring campaigns of the behavior intervention package are introduced in a tiered and sequenced manner across the intervention period, and are designed to coordinate with the integration themes presented in Table 2. The self-monitoring campaigns follow a consistent structure within each semester, while the thematic content or focus shifts across semesters.

Within each semester of the intervention period, a self-monitoring campaign consists of classroom-based activities integrated within and building upon the prior FLASH classroom activities. Each activity lasts 15-20 minutes and uses a self-monitoring vehicle such as tickets. Each campaign starts with establishing the rationale for self-monitoring. Students increase self awareness throughout the activity:

1. They first indicate current (or ‘baseline’) levels of the targeted behaviors.
2. They then work through a ‘personal challenge’ in which youth are provided information on the target behavior to guide them in setting personal goals for behavior change. Students are challenged to alter (increase or decrease, as applicable) the target behaviors according to their personal goals.
3. The campaign ends with a ‘group challenge’ or competition in which students compete as teams to see which groups achieve the greatest behavior change in the desired direction.

Throughout, youth may be given small giveaway items or social recognition and rewards to reinforce behavior change and self-monitoring activities. They are provided with group feedback about their efforts.

Self-monitoring campaigns engage increasingly large groups of students over the course of the trial to sustain participant engagement, to maintain momentum and enthusiasm within schools, and to capitalize on developmental changes in middle school youth. As feasible, group competitions become progressively bigger in scope/geographic reach across time, building from the simplest level of classroom competitions (in 6th grade) and culminating with a national multi-center competition (in 8th grade). Campaigns are designed to be consistent with school and district policies. Group contests are structured to eliminate use of any identifiable individual data; aggregate data are used to protect privacy and confidentiality (e.g., average servings of water, average decrease in screen time). Additionally, teachers, staff, parents, and administrators are encouraged to participate in the campaign as positive role models for the importance of healthy lifestyle behavior change.

6.3.2.3 Family Outreach

Family outreach involves distribution of newsletters, other written communications, and possibly events or activities which provide the following opportunities:

- Inform parents about the intervention components and goals. Newsletters contain information about the value of recommended behaviors (e.g., increasing water intake, increasing physical activity, reducing sedentary behavior) and the nature of the physical education, nutrition, and behavior intervention components at their local school.
- Involve families in the dissemination of the intervention messages. Newsletters feature elements about and/or contributed by actual parents at the school (such as jokes, recipes, or tips). Suggestions are made about how to stimulate communications between parents and children related to the behavior goals.
- Provide continued exposure to intervention messages during school breaks and vacations.

Study staff develop newsletter contents. A template layout is created for insertion of local text and pictures. Student peer communicators may be asked to perform as 'photo-journalists' or reporters taking pictures, collecting stories, recording student quotes, and generating captions during study-related events. First person narratives of parents dealing with health-related choices and changes are derived from two parent focus groups per field center per year. The HAT is also used to provide advice and support for both the newsletter and participatory events.

In addition, parent reaction to family outreach events and activities is gathered in focus groups; up to two groups of about 8 parents each are conducted at each field center each year of the intervention.

6.4 School-wide Communications

Together, the Prevention Communications Committee and the Communications Core develop materials, activities, and messages that motivate students and build excitement within the student population around behavioral goals for each semester's intervention, and for healthier behaviors generally. Communications activities, messages, and support materials promote the benefits of and attempt to lower some key barriers to targeted physical activity and dietary changes.

Communications are delivered in unified campaigns. There is one campaign for each intervention theme (see Table 2) as well as for recruitment and retention efforts. The campaigns tie together all communication elements, maximize the impact of the communications, and establish a common theme across all study materials. Materials match closely the identified needs of the committees involved in the intervention (Behavior, PE, and Nutrition/Food Service) as well as Recruitment and Retention.

The study has chosen "HEALTHY" as its identity. The identity is the study's public face or brand, and becomes the one consistent and unifying factor for all study communications materials and messages regardless of audience, venue, or time. The identity conveys the essential characteristics of the study as a memorable and appealing name and graphic representation (logo), which then becomes

the identifying element on all communications materials. The identity, coupled with the communications campaign, provides a look and feel that helps to unify and integrate all study activities, including the multiple interventions and activities related to each semester's theme, recruitment, and retention. The name and other materials and messages are developed for all sites to use for recruitment and the launch of the study as well as to reinforce core behavior change goals.

While the project identity and communications campaigns are developed first and foremost to build awareness and motivation for core behavior changes among students, the project identity and materials must also be acceptable to the other target audiences for the project including NIH/NIDDK, the collaborative study group, study school districts, school personnel, and students' families.

6.4.1 Overview of Goals and Strategies

The goal of school-wide communications is to make HEALTHY fun and exciting for kids and a positive reinforcement for adults. Activities, messages, and materials are designed to motivate and engage students in ways that make students (1) more receptive to behavioral, nutrition, and physical activity changes introduced by the intervention and (2) more likely to internalize healthier behaviors outside the classroom and cafeteria environments.

Motivational activities support and extend the two main environmental interventions (nutrition/food environment and physical education), the behavior interventions (FLASH, self-monitoring campaigns, and family outreach), and recruitment and retention. Across the intervention period, school-wide communications promote targeted changes in students' physical activity and diet behaviors, namely, increasing healthy behaviors (e.g., increasing water, fruit, vegetable, whole grain consumption, and physical activity) and decreasing unhealthy behaviors (e.g., decreasing sugar added beverage, other unhealthy food consumption, and screen time).

To achieve optimal engagement within the intervention student population, the communications plan offers a fully supported menu of:

- core materials and actions,
- events designed to offer sites regional, cultural, and operational flexibility, and
- premiums, i.e., small items given to all students that support the event and core options chosen for that semester's intervention theme.

Study staff leads a team of student peer communicators at each site who help select each semester's event(s) and premium choices to allow operational, developmental, and regional customization. This framework is designed to offer maximum buy-in to students. In addition, they provide an informal avenue for getting student feedback about how well communications activities are targeting the needs of the students (e.g., are developmentally and culturally appropriate) and inform any refinement made to the communications campaign during the course of the trial.

No intervention-related communications activities take place until initial recruitment has been completed. The Communications Core at Planit designs and develops materials in collaboration with the Communications Committee. The core uses insights gleaned from consumer research to position target behaviors more attractively to the study stakeholders (students and their families, school personnel, and the study staff).

Addressing the normative environment in each school is a particularly critical objective of the school-wide communications campaigns. Encouraging participation and endorsement and neutralizing resistance among influential older students is particularly important. The goal is for staff, older students, and those peers most likely to be influential among large constituencies of the school population to model and encourage the desired behaviors for students generally (and younger students in particular) to believe that "if this is the way these things are done at my school (or among my peers), then this is how I'm expected to act, too".

School-wide communications campaigns and messages are designed to reflect the main themes of the project. To achieve maximum identity, the HEALTHY brand or logo is used in all

communication materials. As possible, the HEALTHY logo is also used to co-brand the PE equipment, food packaging, and other tangible materials used/distributed in the intervention schools.

6.4.2 Schedule and Delivery

The field center project coordinator oversees implementation of recruitment and retention materials, and the health promotion coordinator (HPC) oversees implementation of school-wide communications materials related to the intervention. The core set of school-wide communications materials are available with a common look and feel for use throughout the school. They are used according to a schedule coordinated with the integrated themes phased roll-out. The additional elements (events and premiums) are chosen by each school's student peer communicators, in collaboration with study staff, from a short menu of options early in the intervention semester. Schools are encouraged to maximize use of all available materials and events for study promotion.

The Communications Committee supports (1) training, materials supply, and support for student peer communicators and (2) study elements that are both motivational and instructional, including (but not limited to) cafeteria learning materials, newsletters, incentives, and flyers.

7 MEASUREMENTS AND EVALUATIONS

7.1 Primary and Secondary Outcome Measures

This section presents the schedule of data collection and procedures and instruments used, with appropriate supportive evidence, justification, and validation. Primary and secondary outcomes are measured per student unless otherwise indicated:

<u>Primary</u>
1. BMI percentile* (BMI determined by height and weight, percentile adjusted for gender and age)
2. fasting glucose (mg/dL)
3. fasting insulin (μU/mL)

** outcome for which the study is powered*

<u>Secondary</u>
1. lipids (total cholesterol, HDL, LDL, triglycerides)
2. other laboratory indicators of diabetes and obesity risk, such as HbA1c
3. blood pressure
4. waist circumference
5. physical activity
6. sedentary behavior
7. fitness
8. daily nutritional intake
   (a) calories overall and from specified food groups
   (b) percent calories from fat
   (c) servings of fruits, vegetables, high fiber grain based foods, high fiber legumes
   (d) water
9. FLASH self-assessment scores
10. PE class activity level (MVPA by heart rate monitor)
11. quality-adjusted life years saved (QALYS)
12. total school food environment amounts and nutrients
    (a) kilocalories
    (b) fat
    (c) fiber

(d) fruits and vegetables
(e) dessert and snack food
(f) beverages (milk, added sugar, juice, water)
(g) grain-based foods and legumes

13. grade and school level state standardized test score pass rates
14. grade and school level attendance rates
15. grade and school level comportment rates (i.e., referral to administrative offices for disciplinary action)
16. costs associated with intervention delivery and administration
17. decisions, policies, and activities at the school, local, state, or federal level that influence the school environment for nutrition and physical activity

Two additional types of data are collected: (1) demographic data and individual characteristics and (2) process evaluation data. The following demographic and descriptive data are collected: gender, age, race, ethnicity, socioeconomic status (head of household highest education level), sexual maturity (Tanner stage), family history of diabetes, and child's medical history. Process evaluation data are collected in intervention schools only to document and monitor intervention dose, fidelity, and reach.

Intervention staff members also collect feedback information on an informal basis to help them with intervention delivery. The methods of collection are typically quick survey or observation related to a specific event or activity, with immediate interpretation and application. Feedback is not considered study data and is not described further.

7.2 Outcomes and Data Collection Schedule

Table 4 lists data collection measures and procedures and indicates during which half-year block they are recorded.

Table 4. Schedule of Data Collection Measures and Procedures

Measures and Procedures	Schedule					
	1st half 6th (base-line)	2nd half 6th	1st half 7th	2nd half 7th	1st half 8th	2nd half 8th (end of study)
Demographic and Descriptive Characteristics						
• sex, date of birth, race/ethnicity	x					x
• socioeconomic status	x					x
• family history of diabetes	x					x
• medical history	x					x
• sexual maturity (Tanner stage)	x					x
Student Physical Measures						
• fasting glucose, insulin, lipids, other labs, banked blood specimens	x					x
• height, weight	x			x		x
• waist circumference	x					x
• blood pressure	x					x
• fitness (20-meter shuttle test)	x					x

Table 4. Schedule of Data Collection Measures and Procedures

Measures and Procedures	**Schedule**					
	1st half 6th (base-line)	**2nd half 6th**	**1st half 7th**	**2nd half 7th**	**1st half 8th**	**2nd half 8th (end of study)**
• adverse events	x					x
Student Self-report Behaviors						
• diet/nutrient intake (FFQ)	x					x
• physical activity (SAPAC)	x					x
• sedentary behavior (SAPAC)	x					x
• FLASH self-assessment scores (a)		x	x	x	x	
Economic Cost-Effectiveness						
• student health-related quality of life	x			x		x
• personnel costs	x	x	x	x	x	x
• PE costs	x	x	x	x	x	x
• school food environment costs	x	x	x	x	x	x
• behavior intervention costs (a)	x	x	x	x	x	x
• communications intervention costs (a)	x	x	x	x	x	x
School Food Environment						
• ordering, production, and sales records	x			x		x
• record of vending machine contents	x			x		x
• item-based nutrient analysis	x			x		x
PE Activity Level						
• MVPA (heart rate)	x			x		x
School Academic Performance						
• standard test scores	(b)	x		x		x
• attendance	(b)	x	x	x	x	x
• comportment	(b)	x	x	x	x	x
Environmental Influences						
• decisions, policies, mandates, changes		x		x		x
Process Evaluation (a)						
• observation PE class		x	x	x	x	x
• percent student participation in PE		x	x	x	x	x
• review PE intervention delivery		x	x	x	x	x
• observation food environment changes		x	x	x	x	x
• review nutrition intervention delivery		x	x	x	x	x
• percent participation in FLASH		x	x	x	x	x
• proportion FLASH delivered		x	x	x	x	x
• observation FLASH in-class		x	x	x	x	x
• review behavior intervention delivery		x	x	x	x	x
• peer communicator activities		x	x	x	x	x

Table 4. Schedule of Data Collection Measures and Procedures						
Measures and Procedures	**Schedule**					
	1st half 6th (base-line)	**2nd half 6th**	**1st half 7th**	**2nd half 7th**	**1st half 8th**	**2nd half 8th (end of study)**
• peer communicator focus groups		x	x	x	x	x
• use of communications materials		x	x	x	x	x
• student recall messages and activities		x	x	x	x	x
• school administrator interview		x		x		x
• integration management survey		x	x	x	x	x

(a) intervention schools only
(b) baseline measures of academic performance are collected for school year 2005-2006

7.3 Procedures and Instruments

7.3.1 Demographics and Descriptive Characteristics

Students provide sex, date of birth, and race/ethnicity by self report.
Parent/guardian completes a self report form with items for:

- socioeconomic status, i.e., highest level of education attained by head of household;
- family history of diabetes in first degree blood relatives;
- medical history of the child, i.e., diagnosis of diabetes and current medications.

Data are collected at baseline and at end of study, when additional students are recruited for measurement.

7.3.2 Health Screening

7.3.2.1 Anthropometrics, Blood Pressure, and Fasting Blood

Measurements are made by trained staff who use standard equipment and adhere to calibration procedures provided by the study. Students are instructed to wear light, loose-fitting clothing. To ensure privacy, measurements are made behind a screen. Height and weight are measured without shoes. Blood pressure is measured at 3 points, the first taken after the subject has been sitting quietly for at least 5 minutes and the second and third taken at least 1 minute apart. Blood pressure is measured using an automatic inflatable digital blood pressure monitor with variable cuff sizes. Waist circumference is taken on bare skin measured just above the iliac crest.

Fasting blood is drawn to determine insulin, glucose, and lipids, as well as provide stored samples for later evaluation. The evening before data collection, the study staff calls the students scheduled for the next day's blood draws to remind them not to eat any food or drink anything except water after midnight, not to eat breakfast, and to wear comfortable loose-fitting clothing. Parents are asked to bring their children to school early the next morning and have them report to the area designated for data collection. Standard procedures are followed by licensed phlebotomists with experience working with children. A study physician is available by phone in case of adverse events. A numbing cream may be applied with adequate approval. Approximately 20 mL (about 4 teaspoons) blood is drawn at each data collection, half for immediate analysis of study outcomes and half for storage. Tubes are labeled with the child's study ID number. Blood is processed, handled, stored, and shipped following instructions provided by the central blood laboratory.

7.3.2.2 Sexual Maturity (Tanner Stage)

Sexual maturation or pubertal stage is determined using the Pubertal Development Scale (PDS) [Petersen et al. 1988], a self-administered questionnaire that has been widely used as a non-invasive indicator of pubertal status [Petersen et al. 1983; Robertson et al. 1992]. The PDS has two 5-item subscales, one for each gender. The subscales consist of specific developmental characteristics such as growth spurt, pubic hair, and skin change for both boys and girls, facial hair growth and voice change for boys, and breast development and menarche for girls. These are coded on a 4-level ordinal response scale. Tanner score is determined by an algorithm combining the responses. The scale is internally consistent, with alphas ranging from 0.68 to 0.83 (median of 0.77). Adequate correlations have been found between the PDS and physician ratings of sexual maturity based on the Tanner scale (r=0.61-0.67), between the PDS and adolescent self-reports based on Tanner scale pictures (0.72-0.80) [BrooksGunn and Warren 1988], and between the PDS and age at peak height velocity and interviewer assessments of maturity [Petersen et al. 1988]. Further evidence of validity is that the measure reveals expected patterns of pubertal change [Petersen et al. 1988]. The scale is self administered at baseline and end of study.

7.3.3 Physical Activity Intervention

7.3.3.1 Activity Level in PE Class (Heart Rate Monitor)

Activity level in PE classes is collected in both intervention and control schools as a secondary outcome measure at baseline, second semester of 7th grade, and end of study. The data are used to interpret study findings and evaluate the ability of the intervention to attain the targeted level of MVPA. Data are recorded on heart rate monitors worn by consented students during the PE class. The sample of specific classes and students is selected by an unbiased scheme generated by the coordinating center. Measurement times are unannounced to prevent bias in selection of activities by the PE teachers.

7.3.3.2 Fitness (20-Meter Shuttle Test)

The measure of fitness is based on the number of laps completed during the 20-meter shuttle test (20-MST) [Leger and Lambert 1982; Tompkinson et al. 2003]. Although there are a number of other modalities to assess fitness, the other testing methods are either too challenging for children or require expensive equipment. The 20-MST (1) can be accomplished in available school space [Klissouras and Tokmakidis 1982; Baquet et al. 2001; Guerra et al. 2002], (2) can be administered to a large number of youth within a single class period, and (3) requires no specialized equipment other than a tape/CD player and stopwatch.

The test requires the subjects to run back and forth between two lines set 20 meters apart. The running pace is determined by audio signals emitted from a pre-recorded CD. The initial velocity is 8.5 km/h, and the velocity increases by 0.5 km/h every minute. The test is completed when the participant is not able to complete the distance at the stipulated pace on two laps. A score for the test is assigned based on how many stages and laps were completed. Leger et al. [1988] also used number of laps completed to compute a measure of maximal aerobic power (cardiorespiratory fitness, or VO_2max). The test was initially validated by Leger et al. [1988] but has been validated a number of times by other investigators. Boreham et al. [1990] validated this protocol against the PWC test and a VO_2max test in a sample of high school students and found a high correlation, r=0.87. This test has also been validated against VO_2max in a sample of 103 twelve-year-old non-Caucasians with r=0.83 for boys and r=0.76 for girls. The reliability of the test was r=0.73 for boys and r=0.88 for girls [Mahoney 1992]. The 20-MST has been used successfully in large school-based population studies

[Baquet et al. 2001; Guerra et al. 2002] and seems a sensitive tool to assess improvement in aerobic power in youth.

All students participate in the 20-meter shuttle test (20-MST) during PE classes at baseline and end of 8th grade. Study staff not involved in the intervention delivery administer the test and record outcome data; however, data are used only for those students providing consent/assent.

7.3.3.3 Self-report Physical Activity and Sedentary Behavior (SAPAC)

There are a number of self-report questionnaires used to obtain information on physical activity patterns in adolescents. This trial uses the 2-day version of the Self-Administered Physical Activity Checklist (SAPAC) [Gilmer et al. 1996; Sallis et al. 1993, 1996] to estimate physical activity levels and sedentary behaviors. SAPAC is an activity-based self-report measure. The instrument is structured around a list of activities with minimal cues about the time of day. The respondent reports minutes per day of the specific activity performed over the previous two days. The SAPAC also includes information of sedentary activities, including television and video viewing, computer time, reading and homework, telephone time, and hanging out with friends.

McMurray et al. [2004] compared two different survey methods to each other and to physical activity measured by accelerometry. They reported that the overall 2-day test-retest reliability correlation was 0.67. The correlations for MVPA comparing different survey methods and accelerometer counts measured for 3 days were generally poor, favoring neither type of recall. However, correlations for vigorous physical activity and accelerometer counts were higher for an activity-based approach (SAPAC) than for a time-based (PDPAR) approach ($r = 0.281$ vs. 0.162).

7.3.4 Nutrition Intervention

7.3.4.1 Self-report Diet/Nutrient Intake (FFQ)

Students self report dietary intake using a semi-quantified food frequency questionnaire which solicits information from the past week. Food frequency questionnaires (FFQ) are the most commonly used tool in nutritional epidemiology and have contributed greatly to the understanding of many diet-disease associations. Research has shown that nutrient intakes assessed by standardized food frequency questionnaires are reasonably correlated with those from more detailed methods and thus provide a valid representation of usual intake for ranking subjects [Willet 2000]. Because food frequency questionnaires can be self-administered, they provide a method of collecting data that is relatively low cost for large population studies.

The Block Kids FFQ asks about approximately 100 food items. It solicits information concerning portion sizes using a serving size visual. The original questionnaire [Block et al. 1986] was validated in numerous studies and in a variety of populations [Block and DiSogra 1995; Block et al. 1990, 1992, 1994] and has been redesigned for use with children. A small validation study was conducted among seventy-four 8-10 year old African-American children attending school in Philadelphia; the comparison tool was one 24-hour dietary recall. Correlation coefficients ranged from .40-.50 for total energy, fat, saturated and monosaturated fat, carbohydrate, fiber, and calcium [abstract presented at the 4th International Conference on Dietary Assessment Methods].

Standard software is used to analyze the data collected. The software determines estimates of usual intake for a variety of nutrients, including calculations of daily frequency and amounts for individual food items as well as by food group.

7.3.4.2 School Food Environment

In order to determine attainment of total school food environment goals, sales and production records for foods and beverages from cafeteria meals and programs, a la carte, and vending machines

are collected at baseline and end of 7th and 8th grade school years. Data are collected for 20 consecutive day-long periods. Production records and meal participation rates are extracted from source documents provided by the food service manager at each school. Sales data are provided by cash register records or by the food service manager at each school, or in the case of snack and beverage vending, by the party responsible for the vending machines (school specific).

Foods are analyzed for nutrient content. Analysis software applies a nutrient database that uses site-specific food and beverage items to produce a data file with complete breakdown of nutrients and food components.

7.3.5 Behavior Intervention

7.3.5.1 FLASH Self-Assessment Score

Self-assessment data are recorded and collected as part of the FLASH in-class activities. There is a FLASH workbook for each campaign or theme. Activities begin with self-assessment to establish a baseline 'score' based on how frequently the student performs or engages in certain behaviors. At the end of the module, the student completes the same self assessment. Change in score pre to post indicates the success of the activities to promote acquisition of critical knowledge and self-efficacy for health-related behavior change. Pirouznia [2000; 2001] has shown a direct correlation between nutrition knowledge and food choices for both boys and girls in middle school. Both male and female subjects' fat and sugar intake are negatively related to their self-efficacy for making healthful food choices [Cusatis et al. 1996] and self-efficacy has been shown to be an important mediator of physical activity among youth [Chase 2001; Johnson et al. 2000].

7.3.6 Economic Cost-Effectiveness

7.3.6.1 Health Related Quality of Life

Economic evaluation of the prevention intervention intends to express the value for cost of the intervention by use of cost-effectiveness analysis. The cost-effectiveness ratio is the cost per quality-adjusted life year (QALY) [Gold et al. 1996]. This ratio reports the cost required to purchase one fully functional year of health. QALYS combine length of survival (mortality) and level of functioning (morbidity) into a single measure. QALY weights generally range between 0 (death) and 1 (perfect health)—e.g., a health state with a utility value of 0.8 indicates that a year in that state is worth 0.8 years with perfect health—but there can be states worse than death (less than 0).

Quality adjusted life year (QALY) is determined by self-report using a validated health-related quality of life instrument. Two instruments are administered: (1) the visual-analog feeling thermometer from the EuroQoL (EQ-5D) preference assessment instrument and (2) the Health Utilities Index (HUI), a preference-weighted health state classification system.

7.3.6.2 Intervention Resource Expenditure and Outlay

Cost data are collected at the school level only—no collection of cost information from students and their parents is planned. The goal is to assess all resource use and costs, regardless of whether a monetary transaction has taken place. The following data are collected:

- Food service: Food, labor, and central kitchen costs assigned to the site; revenues (total a la carte cash sales by day, cash meal and program sales, USDA reimbursements); meal and program participation (total number of serving days, count by day and by free/reduced/paid category); intervention costs (research dietitian salary, training costs, travel costs).

- Physical education: Time PE teachers spend in class teaching students; equipment and supplies; intervention costs (physical activity coordinator salary, PE teacher assistant salary, training costs, travel costs).
- Behavior change: Time classroom teachers spend in class delivering behavior intervention components; supplies; intervention costs (health promotion coordinator salary, health promotion coordinator assistant salary, training costs, travel costs).
- Communications and promotions: Costs related to posted media, such as banners and posters, as well as events and activities.
- Personnel costs: Intervention and research level of effort for study staff.

Total school food environment and physical education cost data are collected at both intervention and control schools; otherwise data are retrieved from intervention schools only. Costs of school environment changes, in-kind donations, and outside grants are also collected.

7.3.7 School Academic Performance

Although the potential health benefits of the proposed intervention are extremely important, scholastic excellence is the primary purpose of schools. If the intervention is successful but associated with an adverse impact on scholastic performance, it will have little chance of being widely adopted. Scholastic performance includes aggregate academic performance, attendance, and disciplinary actions. These data are collected throughout the study in both intervention and control schools.

Data are collected to document the characteristics of the respective state accountability test and the total number and passing rates of students taking the test. The subject areas of interest are math and reading. These tests are taken by 6th, 7th, and 8th graders in intervention and control schools every year. Grade and school level data are recorded—no individual student data are collected.

In addition, data are collected to determine rates of grade level absences and referrals for disciplinary action. Policy and practice related to disciplinary referrals and any changes are recorded.

7.3.8 Environmental Influence

Changes may occur in and around the school that impact on the school's nutrition and physical activity programs during the intervention period. These influences may occur at either or both control and intervention schools and may be due to federal, state, or local mandates, policies, or decisions. It is necessary to document external independent programmatic, policy, and environmental changes to assess their potential effects. Assessing these potential confounding effects is critical in a multi-year intervention that focuses on the impact of a strong environmental intervention. It is particularly important for this trial because of the increasing national awareness of the prevalence of obesity and low physical activity levels among children and adolescents [Troiano and Flegel 1998]. National recommendations, referenda, and initiatives are ongoing and proposed that can influence the trial's primary outcome in both intervention and control schools.

Data are collected related to physical activity and nutrition that may occur in the school but are not necessarily part of the study intervention, including: (1) aspects of the environment in the school, in the school neighborhood, during school hours, and after or before school, (2) grants and research program initiatives, (3) local, state, or federal mandates, (4) promotions and advertising.

Data are collected at the end of each school year. Data collected relate specifically to the grade involved in the intervention that year. Longitudinal changes from one year to the next or from the beginning of the study to the end as well as group (control vs. intervention) differences can be assessed to help interpret potential changes in study outcomes.

7.3.9 Process Evaluation

Process evaluation takes a broad approach to assesses the extent to which interventions are delivered and received as intended. It assesses *fidelity* of intervention delivery (the extent to which the intervention is delivered as intended), the intervention *dose* (how much of the intended intervention is delivered), and the *reach* to the groups targeted by the intervention (the proportion of intended recipients who actually participate in an intervention). By monitoring the delivery of key intervention components and providing timely feedback to the intervention staff, process evaluation data can be used to help ensure fidelity of intervention delivery. Monitoring and providing feedback on the intervention ensures adequate implementation of the intervention components. Reach provides information on the ability to penetrate the intervention targets. In combination, process evaluation data can be used to help explain study outcomes.

Process evaluation uses both quantitative and qualitative methods, including structured observations, questionnaires, semi-structured interviews, focus groups, and logs. Interviewers take notes during the conversations, and audiotapes may be used as a local option in order to help the interviewer write up notes. The tapes are then destroyed.

Process evaluation is conducted in intervention schools only within a framework of evaluation measures for each of the study's intervention components:

- Physical education
  - structured observation of participating PE teachers in class
  - percent of students in the grade who participate in the study PE classes
  - interview with physical activity coordinator about PE intervention delivery
- Nutrition/food environment
  - structured observation of changes occurring in the total school food service environment
  - interview with research dietitian about nutrition/food environment intervention delivery
- Behavior
  - structured observation of FLASH sessions in-class
  - percent of students who participate in FLASH
  - proportion of FLASH delivered
  - interview with health promotion coordinator about behavior intervention delivery
- Communications
  - review of peer communicator activities
  - focus groups with peer communicators to gain student perspective on performing specific activities and ideas for new/modified activities for subsequent intervention phases
  - number and type of materials used
  - surveys with students to record recall of events, activities, and messages (The survey takes about 5 minutes and is administered one-on-one to a convenience sample of consented students per school, e.g., recruited from classroom or homeroom volunteers as well as areas where students congregate before/during/after school such as after school programs, cafeteria or lunchroom, recess. Surveys are collected from 10% or at least 20 consented students.)
- Overall program
  - interview with school administrator about progress of the program

In addition to on-going process evaluation, efforts are made as the study winds down to learn from various school staff and personnel their overall perspectives about the HEALTHY interventions, strengths and positive effects, weaknesses and problems, and plans for sustaining the program. A sampling of staff and personnel are invited to participate, including PE teachers, FLASH teachers, food service staff, administrators, and students. Individuals may either be interviewed, participate in

a focus group, or complete a self-report survey. Interviews would take one-half hour or less and surveys would be no more than 10 minutes. Informed consent is obtained as appropriate.

8 PERSONNEL AND TRAINING

The study involves personnel from the study field centers (study staff) and from the school environment. Training workshops are held in order to assure that the study is conducted in a standardized manner across all participating centers.

8.1 Study Staff

Study staff is divided by task into those assigned to (a) general oversight and management functions and performing study evaluation and data collection procedures and (b) implementation and delivery of the intervention. These two functions are separated in order to help ensure objectivity. Among those on the field center staff, some are assigned to each school and some have duties spread across schools.

(a) Study staff involved in management and oversight functions include investigators, project coordinators, school coordinators, research assistants, and—as needed—interviewers and certified phlebotomists and nurses.

(b) Study staff involved in intervention conduct and delivery are specialists with relevant educational backgrounds and experience:
- The physical activity coordinators (PAC) work with the PE teaching teams at the intervention schools to assist in the implementation of the program by conducting training, developing strategic plans jointly with the PE teacher, and providing guidance.
- The PE teacher assistants help the PE teacher deliver the intervention. They are hired by the field centers and at least one is assigned to each intervention school.
- The research dietitians (RD) work with the school food service workers and management to monitor and assist with study changes to the nutrition/food service environment in the intervention schools, develop strategic plans jointly with the food service manager, and conduct training sessions for the school food service staff.
- The health promotion coordinators (HPC) are responsible for the implementation of the behavior and communications component in the intervention schools.
- The HEALTHY assistants work with the study staff to facilitate implementation of the various intervention components, especially behavior and communications activities including supervision of the student peer communicators.

8.2 School Personnel

Individuals associated with the school are engaged and recruited as follows:

- Administrators. District administrators or superintendents as well as school principals and vice-principals provide approval, support, and guidance.
- PE Teachers. The PE teachers in the intervention schools are the major delivery vehicle for the PE class intervention and meet with the PAC to establish plans and evaluate progress. All PE teachers with students in the grade currently targeted by the intervention are considered participants.
- Food Service Staff. The food service directors and managers in the intervention schools meet with the RD on a regular basis to plan and monitor the implementation of the environmental changes and targeted goals. Food service workers in the intervention schools attend local training sessions conducted by the RD and other study staff designed to explain the purpose of the study and the intervention. Their buy-in helps intervention components designed to

provide healthier food offerings and preparation and promote enhancements to the total school food environment.

- Classroom Teachers. Selected classroom teachers in the intervention schools are integrally involved in the delivery of various behavior intervention components, including FLASH and self-monitoring campaign activities and information. Efforts are made to recruit and train as many teachers as possible at each site, however availability is ultimately determined by each school. Classroom teachers complete a tracking log to document their delivery of the behavior intervention. Teachers may also be involved in the behavior self-monitoring activities and group competitions which are otherwise implemented and monitored primarily by the HPC in a classroom or group assembly context.
- Student Peer Communicators. Student peer communicators are identified in each intervention school and recruited to bolster or complement the core intervention strategies. They disseminate study messages, facilitate specified activities, and serve as 'student advisors' to study staff designing activities for subsequent intervention phases. At the start of each school year, a process involving nominations from students, school staff and faculty, and the local study staff followed by random selection of willing nominees is designed to enlist approximately 10-20 students (depending on school size, about 1-2 students for every 25-30 students in the grade) to serve as peer communicators for the remainder of the school year. A successful peer communicator is not necessary considered to be the ideal role model or student leader, but is described as usually happy, with a good sense of humor, and able to make new friends easily. They are comfortable speaking to other students individually, in small groups, and in larger group settings. They are considered trustworthy and are listened to by other students, teachers, and adults, and they are known to follow through with commitments and assignments. The list of nominated students must be approved by the school principal or designee, who collaborates with study staff on final selection of individuals. One goal in selecting individual peer communicators is to generate a group of students who as a whole represent school-wide student body characteristics.

  Student peer communicators receive training by study staff to enhance skills at delivering announcements with public address systems or classroom-based presentations, interpersonal communication, and other modes of communication. Training is offered after baseline measurements are completed before or early in the 6th grade intervention and in the first 3 weeks of the school year in the 7th and 8th grades. The time and location of the training sessions are pre-determined jointly with the local school principal and staff. Additional activity-specific training is provided during the semester as needed at a time closer to the event. Specific activities and assignments are guided by three general principles:

  - The student may agree to continue or discontinue in this role at any time. Students who do not perform satisfactorily in the opinion of the study staff in joint consultation with the classroom teacher are excused from service.
  - In order not to overextend or burden the student, assigned study-related responsibilities and activities require no more than 1 hour per week on average during any phase of the intervention.
  - Assigned activities are individualized to accommodate the student's strengths and comfort level, and school resources and priorities.

  Student peer communicators collaborate with the study staff to determine which activities work best within their school environment and to guide development of activities for subsequent intervention phases. The students share several messages conveying the overall goals of the project among their classmates. These messages are prepared by behavioral and communications experts on the study team and are consistent across all sites (and schools). Student peer communicator activities may include any of the following:

  - Delivering announcements using school-wide public address systems and/or classroom-based presentations.
  - Distributing study-related messaging premiums associated with promotional events and activities.
  - Assisting study staff with activities related to nutrition, PE, and school-wide communications intervention components.
  - Serving as a photo-journalist or reporter for the family outreach newsletter.
  - Working with HPC and HEALTHY assistant in the homeroom or classroom setting on other study related activities.
  - Assisting the HPC, HEALTHY assistant, and other study staff with school-wide communications events.

  Student peer communicators may be supplied with special branded messaging items to wear (e.g., shirt, vest) during their study activities.
- Health Action Team (HAT). A Health Action Team (HAT) is identified in each intervention school to act as an advisory body, assisting study staff to adapt the intervention materials and activities to the school's specific needs. The HAT is a group of key individuals at the school who provide insight into the social and organizational climate of the school and readiness for implementing the proposed activities. Membership includes representatives from faculty, administration, staff, and parents. Such a group may already exist or need to be established. They meet with study staff 2-4 times per year.

8.3 Training

All study staff and participating school personnel must attend training sessions provided by the study and delivered centrally, regionally, or locally. Investigators, study staff, and additional experts provide instruction on various aspects of the study. Training is based on the study manual of procedures. Training focuses on function and role and may include background and rationale, study design, intervention implementation schedule and procedures, data collection and management procedures, communications and motivational skills, and maintaining privacy and confidentiality. Certain procedures involving use of specialized data collection procedures, equipment, or technology may require that the trainee pass certification criteria established by study experts. All training sessions provide time for Q/A and discussion of barriers and their resolution. Booster sessions are planned. The need for additional training is also evaluated on a case-by-case basis.

The coordinating center holds an initial and subsequent booster training workshops for study staff in order to assure that the study is conducted in a standardized manner across all participating field centers. In addition, a single, simultaneous training workshop for all study staff maximizes uniform understanding of study goals and procedures and encourages team building. Central training sessions include preparing study staff to train local school staff.

Certain ancillary study staff—including research assistants and HEALTHY assistants—attend local or regional training sessions.

Study staff conduct training sessions for school personnel. This training is presented in more detail:

- The training program for the PE teachers and teacher assistants is delivered by the physical activity coordinator. The training program occurs in four phases. Phase 1 is an introduction to the study for all PE teachers in the school (1 hour orientation). In phase 2, the physical activity coordinator observes each participating PE teacher during PE classes in order to understand the PE teacher's approach to teaching, strengths and weaknesses, and local barriers to enhancement of PE classes. Phase 3 is a 6-hour workshop for the specific teachers and teacher assistants involved with the intervention focusing on t he unit plans and teaching

skills. The 6-hour training not only introduces the units and lesson plans, activities, and equipment, but covers how to create a safe learning environment, successful instructional strategies to increase activity and participation, motivation and behavior issues, and promoting physical activity outside the classroom. In phase 4, the physical activity coordinator interacts with the PE teacher in and out of the classroom throughout the school day to improve managerial, motivational, and other techniques (12-15 hours). In addition to the initial training, PE teachers and teacher assistants also attend a 6-hour booster training session held in the second half of the school year and also conducted by the PAC. The 6-hour booster training sessions are designed to keep the local PE teachers and teacher assistants on task, to promote teacher and assistant skills, to bring about behavior change in methods of administering the PE program, and to address intervention delivery issues and barriers. New PE teachers who join mid-year are given one-on-one training by the PAC.

- The first stage of the nutrition intervention is school food service staff training conducted locally by the research dietitian.

  For *intervention schools*, the initial training session takes 4-6 hours. Background information is provided about the increase in childhood obesity and the accompanying increase in incidence of type 2 diabetes in the United States. The trial is described including goals, objectives, and intervention strategies. A standard sequence of training activities is then completed and repeated for the portions of the intervention dealing with cafeteria meals and programs, a la carte, and vending machines. Within each area, training includes taste tests, if possible, to make people comfortable and to introduce examples of the food item changes being suggested. The research dietitian reviews the targeted primary outcomes, and training then focuses on customizing the intervention to address deficient areas in each school. Specific changes for food offerings are described, incremental steps to meet target goals are planned, and concerns about implementation of changes are discussed and addressed with food service managers and workers. Changes in the total school food environment are also targeted in the intervention. Methods for altering the food environment are described. Barriers to implementation are discussed along with methods for overcoming these barriers. Finally, study data collection procedures and data forms are reviewed. Two-hour booster training sessions are held at the beginning of each subsequent semester to refresh and remind about the intervention, familiarize new hires, discuss goals and changes for the coming year, and address any concerns or problems.

  For *control schools*, food service managers and staff attend annual 2-hour orientation sessions to introduce, familiarize, and discuss study procedures performed in control schools—namely, data collection.

  Staff training is attended by food service managers and workers. Food service directors are invited to attend all staff training sessions (without compensation). Intervention school directors are also invited to meet together with study nutrition intervention staff in orientation sessions to discuss overall strategies and implementation.

- Classroom teachers are trained by the HPC in the scope, sequence, and methods of facilitating the FLASH and self-monitoring activities. The training time for these activities is 4 hours per year in the 1st half of the school year and an additional 1-hour booster training per year in the 2nd half of the school year.

- The HPC, HEALTHY assistant, and other study staff conduct training for student peer communicators. The initial training is conducted in 1-2 sessions lasting no longer than one hour each. Training is provided to familiarize students with the required tasks, skills, and procedures. Training is offered in the first 3 weeks of the first intervention phase each year at a time and location pre-determined jointly with the local school principal and staff. An

additional 2-4 20-minute activity-specific refresher training sessions are provided to individuals and small groups of peer communicators just before the activity takes place.

- The first meeting of the Health Action Team (HAT) includes a training session conducted by the study staff. The training provides an overview of diabetes prevention, the purpose of the trial, and description of the intervention components before focusing on the role and responsibilities of the HAT.

8.4 Human Research Subject Certification

As noted, participating schools operate under Federal Wide Assurance (FWA) to conduct research, and various school personnel—including classroom teachers, food service staff, PE teachers, and student peer communicators—are considered agents of the study and may assist in the delivery of selected intervention components. Given the trial design, the number of individuals involved, and the inclusion of minors, the process of certification of individuals is difficult and impractical. In addition, these individuals are not members of the target audience for whom this training was intended—i.e., they are not researchers or investigators, they become involved after the protocol has been finalized, and they have no influence, control, or responsibility for study design. Each field center seeks exemption in the IRB submission from the requirement of human subjects certification for these individuals. Study conducted training sessions emphasize privacy and confidentiality of subjects and data.

9 SAFETY REPORTING AND MONITORING

Protection of participants from risks related to the study is an overriding concern to study investigators. Each of the field centers must seek site-specific Institutional Review Board approval for the protocol. Appropriate Federal Wide Assurance of protection for all research conducted at the schools must also be obtained. A signed and dated statement that the protocol and informed consent form have been approved by the local Institutional Review Board is forwarded to the coordinating center.

This section pertains only to student participants. The study foresees no measurable risks or benefits nor the occurrence of adverse events to the schools, school personnel, or parents.

9.1 Data Safety Monitoring Board (DSMB)

A Data Safety Monitoring Board (DSMB) consisting of appropriately qualified independent experts is appointed to provide review of data on patient safety and study progress. The purpose of the board is to assure independent review as to whether study participants are exposed to unreasonable risk because of study participation, and to monitor study progress and integrity. Board members are chosen by NIDDK. The DSMB convenes on a regular basis to review study progress and safety. Process evaluation data are presented and used to monitor study progress and feasibility. Interim outcome data analyses is planned following 7th grade data collection (see below).

Adverse event data are collected on study forms. Field centers report adverse events to the coordinating center in a timely fashion, including a narrative summary of the event as well as indication of the duration, perceived relationship to the study procedures, and resolution.

Serious adverse events are reported immediately to the coordinating center which notifies the NIDDK project officer, study chair, and DSMB chair. An unscheduled conference call of the DSMB is convened if needed.

Only fasting blood draws are anticipated to result in the occurrence of reportable adverse and serious adverse events related to this protocol.

9.2 Adverse Events and Serious Adverse Events

NIH guidelines indicate that an adverse event is any untoward medical occurrence in a study participant. We are operationally defining a serious adverse event (SAE) as any event that occurs during the administration of or as a result of the health screening blood draw and causes bodily or psychological damage involving on-site presence of emergency medical personnel (i.e., not just the school nurse). All deaths of consented students are reported no matter when they occur.

On-site study personnel have access to the study adverse event forms and immediately record the information. They notify the field center project coordinator and principal investigator that an event has occurred. Serious adverse event reports are transferred to the coordinating center immediately, which in turn forwards them to the study chair, NIDDK project officer, and DSMB chair. Adverse event data are transferred on a timely basis along with other study data.

9.3 Risks, Risk Management, and Procedures to Minimize Risks

9.3.1 Health Screening Physical Measurements and Forms

The risks related to drawing blood are as follows: brief discomfort from the venipuncture, small bruise at the area of the venipuncture, dizziness or brief fainting, and mild nausea (upset stomach). To avoid and minimize these risks, only people trained and experienced in blood drawing techniques are allowed to draw blood. Venipuncture is done following standard, sterile procedures that include: using a new sterile needle for each blood draw, wearing surgical gloves, placing all needles and items with blood in proper containers that are taken away by the investigators for proper disposal. Application of a skin-numbing cream prior to the venipuncture is available. A physician is available by phone at all times during data collection involving blood draw. The students are given a healthy breakfast following the fasting blood draw.

For students identified as having diabetes, there is minimal risk to coming to school in the fasting state and having withheld their morning medication until their blood is drawn and they are able to eat breakfast. This procedure is routinely done for children with diabetes during their health care visits, and it is anticipated that youth with diabetes and their families are familiar with the procedure. Once blood is drawn, students can go to the school nurse or office where they routinely manage their diabetes, check their blood glucose level (a routine procedure before eating breakfast), and take their medication as indicated. They can then return and eat breakfast with the remainder of the group. They are not identified to the rest of the students as having diabetes. All precautions are taken to identify and treat hypoglycemia if it develops. A source of oral glucose is available. If the student requires administration of oral glucose prior to the blood draw, blood can still be obtained since their glucose and insulin levels are not used in the main analysis. A portable glucose monitor is available if the nurse decides immediate blood sugar results are needed.

To avoid discomfort and protect privacy, the anthropometric measurements (height, weight, waist circumference) are made and recorded behind a screen. The student does not disrobe.

For all self-administered questionnaires, surveys, and forms, students are spaced apart, only the study identification number is recorded, and copies are collected directly by study personnel. Only the sexual maturation questions on the Pubertal Development Scale are anticipated to cause some psychological discomfort and embarrassment.

As a follow-up to the health screening, parents are given written results of their child's physical assessments at baseline and end of study (BMI, blood pressure, fasting glucose, lipids) with ranges and interpretation. Where considered necessary for the child's health, study staff initiate follow-up contact and recommend action as needed. Table 5 gives range categories for this population and indicates values that trigger action.

Table 5. Ranges for Health Screening Measures

Measure	Ranges		
Height (inches)	varies		
Weight (pounds)	varies		
Body mass index percentile	underweight:	< 5%	
	acceptable:	5-84%	
	overweight:	85-94%	
	obese:	≥ 95%	
Blood pressure (mm Hg)		6th grade	8th grade
• systolic	normal:	< 120	< 125
	elevated:	120-150	125-150
	alert:	*> 150 (c)*	*> 150 (c)*
• diastolic	normal:	< 80	< 80
	elevated:	80-95	80-95
	alert:	*> 95 (c)*	*> 95 (c)*
Fasting glucose or blood sugar (mg/dL)	normal:	< 100	
	prediabetes:	100-109 (b)	
		110-125 (b)(c)	
	alert (diabetes):	*> 125 (a)*	
Total cholesterol (mg/dL)	acceptable:	< 170	
	borderline:	170-199	
	abnormal:	> 200	
	alert:	*> 300 (c)*	
High density lipoproteins or HDL (mg/dL)	acceptable:	> 35	
	borderline:	30-35	
	abnormal:	< 30	
Low density lipoproteins or LDL (mg/dL)	acceptable:	< 110	
	borderline:	110-129	
	abnormal:	> 130	
	alert:	*> 190 (c)*	
Triglycerides (mg/dL)	acceptable:	< 130	
	borderline:	130-150	
	abnormal:	> 150	
	alert:	*> 500 (c)*	

(a) Parents are notified of test results indicating diabetes by phone within 48 hours. A study team health professional calls the parents and follows up with a letter providing more information about interpretation and recommended action.

(b) The parent letter interpretation notes that this is a high level, though not indicative of diabetes, and needs to be followed up with evaluation by a health care provider.

(c) In case of abnormal values, then a health professional on study staff calls the parents as soon as possible, usually within 5-10 days. The health care professional provides information about interpretation and recommended action, including recommending that the family should contact a physician for further testing and diagnosis. The health care professional answers any questions and provides assistance with accessing free medical care if needed.

9.3.2 Intervention Procedures

As stated above, no reportable events are anticipated due to the intervention components and procedures and their implementation and conduct, as described below.

Physical Education Intervention. PE class units and lessons are developed consistent with national guidelines and standards. School guidelines are applied regarding exclusion of PE requirement for students who are unable due to a chronic disease or other condition. The study lessons and units are delivered according to state mandated physical education class requirements. Potential risks from the study designed intervention are the same as in a normal PE class, ranging from breathlessness, dizziness, nausea, bumps, bruises, muscle soreness, strains, and sprains to hyper/hypoglycemia or asthma attacks. However, regular physical activity can improve cardiorespiratory fitness and reduce the risk of developing type 2 diabetes and cardiovascular disease mortality over the long term.

Potential risks during the physical education class are minimized by following proper sequencing of exercises. Each class begins with a warm-up to prepare student bodies for more vigorous activity. The activities progress from basic movements to the more complex. The activities are designed with short rest periods and are age and skill appropriate. In addition, the regular PE teacher, who knows the students' capabilities, is presiding over all classes. The PE teacher has discretion to limit any student's participation in which the teacher feels that there is an increased risk to the student. Any injury or complication is immediately reported and action taken dependent upon each school's specific accident/injury response plan.

Nutrition/Food Environment Intervention. The intervention encourages consumption of fruit, vegetables, water, and lower fat foods by increasing the selection of these items in the school food environments. The foods provided in the school are common foods that contain less fat, sugar, and energy. While there are no individual benefits other than healthier food alternatives, the potential benefits to society are great. Risks to participation (such as allergic reactions or choking) are negligible above and beyond the typical risks of eating in the school environment.

Behavior Intervention and Communications. The informed consent and assent forms point out that the individual should not participate in focus groups or interviews if having others learn about feelings or opinions would be embarrassing. No risks or events related to self-monitoring are anticipated. There may be a slight embarrassment if self-monitoring goals set by individual students are not met, but this is minimized by allowing students to set their own goals and monitor their own progress toward meeting them. During classroom challenges, there may be individual embarrassment if a student is perceived as not contributing toward the class goal.

No risks or events are anticipated from student participation in the brief supplemental classroom activities, which take place under normal classroom conditions. Student peer communicator selection procedures involved no risk greater than that due to normal middle school social interaction. Family outreach carries no risk. School-wide communication messages and events carry no risk.

9.4 Risks in Relation to Benefits

One benefit of this study to the parents is the opportunity to receive important health information about their children free of charge. The data collected during 'health screenings', including blood pressure, fasting glucose, and lipids, may reveal an abnormality or troublesome value of which parents, child, and school were unaware. Additionally there are potential health benefits to the parents and children from any changes to healthier lifestyle choices that might occur as a result of the study intervention.

As described above, parents are notified of the possibility of diabetes within 48 hours and other serious abnormalities by phone within 5-10 days. A follow-up letter is sent recommending that they see the child's health care provider. If the child has no regular health care provider, referral to a clinic for further diagnosis and care is made. If the family does not have insurance, the study staff provides a list of referral clinics that provide sliding scale payments.

The potential benefits for science and public health are great. Type 2 diabetes is costly at a societal as well as an individual level, and preventing this disease represents substantial savings. Thus, the benefits outweigh the risks of this study.

10 DATA PROCESSING AND MANAGEMENT

The coordinating center develops and maintains a central database integrating data from the field centers and central cores and laboratories. Qualitative data from process evaluation are accumulated, processed, maintained, and analyzed at the UNC qualitative data core.

Data processing and management at the coordinating center. The coordinating center can accommodate data entered and transferred in a variety of formats. Remote data entry and management systems developed and provided by the coordinating center may be (1) written in commercial data management system software installed on dedicated study computers, (2) accessed from the study secure website, or (3) collected and extracted from devices such as a tablet or palm pilot. Quality control procedures are pre-programmed depending on the technology. These include programmed skip patterns, range checks, and miscodes for multiple choice items.

Data are entered at the remote sites and transmitted to the central database at the coordinating center. Double data entry verification is used if needed to ensure accurate data entry. Data are received from sites in electronic format specific to the technologies and systems in place at each institution. The coordinating center receives data in computer-readable format from the field centers. The coordinating center merges newly received data with the accumulated central database maintained on the Biostatistics Center's server.

Database quality control performed at the coordinating center includes range checks, inter-item checks, cross-table checks, and missing, incorrect, or questionable values. The coordinating center generates queries for the field center regarding data issues and quality. Query edit reports with the necessary patient identifying information and problem values are sent to the field centers for resolution. Corrected values are entered and checked again for consistency with other items. The goals are to make quality control a continuous process, to make the turnaround time between error detection and correction as short as possible, and to document any changes made to the database.

The Biostatistics Center's data backup and security policies ensure the safety and confidentiality of the data. Backup procedures include twice weekly system backup, daily incremental backup, and off-site fireproof storage. Security procedures include logon and link password protection, remote password logon and dial-back modems, and for internet access, separate web servers which use SSL and encryption algorithms. Regularly updated virus scanning software is used routinely to check personal computers for computer viruses. University computing facilities provide support in the event of a disaster.

The coordinating center maintains confidentiality of patient data and emerging results per a confidentiality policy, which every staff member is required to sign annually.

Data processing and management at the qualitative data core. Qualitative data are forwarded to the University of North Carolina at Chapel Hill. Data are coded and analyzed using software programs for text-based data. Members of the process evaluation team develop a codebook jointly for each of the qualitative instruments and additional codes are added as necessary to capture responses to specific questions. Once all responses are coded, text retrievals on specific codes and combination of codes for a particular topic or theme may be performed. From the retrievals, content analysis of

particular topics is followed by displaying data in a series of matrices to facilitate the identification of similarities and differences in themes by field center. This method generates a comprehensive understanding of the identified themes.

All data remain confidential. No individual results are presented. All information collected are kept safe and confidential in a locked file cabinet in the study office at University of North Carolina at Chapel Hill. Only the study staff see this information.

11 STATISTICAL METHODS

11.1 Sample Size

Sample size is determined for the number of schools (clusters) needed in each treatment arm [Murray 1998; Murray et al. 1994]. The following assumptions are made:

- The null hypothesis is no end-of-study difference between intervention and control schools. A specific alternative hypothesis is stated for the primary outcome: the proportion with BMI percentile ≥ 85 is 50% in the control schools and 45% in the treatment schools, i.e., a 10% risk reduction. The value for the control schools is based on results from the OGTT Feasibility Study.
- The analysis adjusts for baseline outcome value. Sample size calculation adjusts for the correlation between baseline and end-of-study values, estimated as 0.9 (derived from UNC CHIC study data).
- Two-sided significant level α=0.05.
- Power is 90%.
- The average number of 8th graders per school in the cohort at end of study is 50.
- Student dropout and withdrawal is primarily for reasons unrelated to the intervention, such as family relocation. (The annual school-wide turnover rate must be ≤ 25% to be included.) These students are removed from the cohort. However, a much smaller percent of students remain in the school but have missing outcome data (e.g., refused measurement, absent on measurement days). These students remain in the cohort and end-of-study outcome values are imputed. Based on study group experience, this percent is assumed to be no more than 5%. For purposes of sample size calculation, we assume a conservative imputation scheme based on control school data. This decreases the detectable difference.
- Intracluster correlation coefficient (ICC) adjusts for the correlation within a single school (between students) compared to across schools. ICC = 0.02 was derived from the OGTT Feasibility Study data, adjusting for gender, ethnicity, and field center.
- Based on the above assumptions, 16 schools per arm are needed. The required sample size of 16 schools per arm is adjusted upward so that there are equal numbers of schools per field center (divisible by 7) and an even number of schools per field center (half randomized to each arm). Therefore, 21 schools per arm are needed for a total of 42 schools.

11.2 Randomization

The coordinating center develops a stratified randomization scheme. The stratification factors are field center and 6th grade size in order to assign comparable within cluster (school) sample sizes across treatment arms at each field center.

11.3 Dropout and Withdrawal

Primary outcome analysis is based on application of intent-to-treat principles. That is, missing end-of-study data are imputed according to conservative and unbiased methods, and subjects (schools and students) are analyzed in the arm to which they were originally randomized.

Monitoring and follow-up of dropouts and withdrawals are described.

School. If a school withdraws, every effort is made to get permission to collect as much data as possible according to the original schedule. However, compromises and negotiations may be made to collect data from a subset of students, to collect partial data (highest priority given to primary outcome), or to collect data on fewer occasions (highest priority given to end of study).

A school assigned to the intervention may withdraw from all or some aspects of the intervention. Again, all efforts are made to keep data collection adherent to the protocol.

Individual school faculty and staff may also withdraw from all or some study procedures.

Reasons for withdrawal are documented.

Student. This section applies to students in the cohort enrolled in 6th grade only.

Student turnover across the intervention is anticipated, with rates varying by school. Student dropout and withdrawal may or may not be related to the protocol events, activities, and procedures.

We assume most students drop out and withdraw primarily due to family relocation unrelated to the protocol. These students are removed from the cohort. A smaller percent of students remain in the school but have missing outcome data (e.g., refused, absent on data collection days). These students remain in the cohort and efforts are made on a one-on-one basis to accommodate data collection. Where possible, end of study data are collected from students who transfer to another school within the district.

Reasons for withdrawal or dropout are documented.

11.4 Interim Analysis and Stopping Criteria

Interim analysis or looks at the data for the purpose of evaluating whether a trial should be continued or terminated prematurely are common features of clinical trials. Such procedures are motivated by the best interests of the participants and by desire to conserve resources, whether the trial is stopped early for futility, for safety, or for significant evidence in favor of the primary outcome. The procedures and criteria for early stopping are established as part of study design and development. The DSMB is charged with monitoring the progress of the research and advising NIDDK on whether to continue or not. NIDDK makes any final decision.

The Prevention Study Group has been charged with extending the methodology of interim or early stopping criteria developed and applied to clinical trials to the primary prevention or cluster design trial. There are no plans to stop the trial prematurely due to extremely significant positive findings. The course or trend in intervention effect is a critical finding, and it would be important to know if the greatest impact on outcome occurs early and then tapers or levels off or if there is a continuous improvement. Criteria are presented for stopping the trial in case of futility or harm.

The stopping criteria are:

1. Failure to recruit an adequate number of schools. If the study does not recruit an adequate number of schools, then the trial will stop. This is determined prior to student recruitment.

2. Failure to recruit an adequate number of students. If the study does not recruit an adequate number of students in the 6th grade, then the trial will stop. This is determined at the end of the baseline recruitment period across all schools.

This criterion refers to having adequate numbers of students in the end of study cohort. Sample size calculations and power assume an average of 50 students per school. An estimated annual attrition rate is available for each school in order to determine eligibility. Randomization of school to intervention or control is stratified by class size within each field center. At the end of 6th grade student recruitment, the estimated attrition rate "r" is used to determine 8th grade cohort size per school:

$$(\#\ 6^{th}\ \text{graders})(1\text{-}r)^3 = \#\ 8^{th}\ \text{graders}$$

The average of the 42 schools must be ≥ 50.

3. Failure to achieve BMI primary outcome in correct direction. If the intervention schools are doing significantly worse than the control schools in percent of students in the cohort ≥ 85th percentile BMI at 7th grade data collection, then the trial will stop. This is determined partway into the 2nd half of 7th grade at the end of interim data collection.

   Alpha spending function methodology appropriate to cluster design trials is applied to protect the significance level at 0.05 overall. We conduct a one-sided test of:
   - H_0: percent in intervention schools with BMI ≥ 85th percentile ≤ percent in control schools, versus
   - H_A: percent in intervention schools > percent in control schools.

   In case of premature termination, all efforts are made to conduct final blood draw and collect primary outcome and other data.

4. Failure to adequately deliver the intervention as planned. Data documenting the delivery and implementation of the intervention by study staff are recorded during the 1st semester of 7th grade. Study-wide delivery efforts and progress must be deemed adequate in order to continue the study.

11.5 Qualitative Data Methods and Analysis

Qualitative data are collected during the trial. The data are used to determine the extent to which interventions are implemented as planned and intended. Results are fed back to intervention staff in a timely way so that adjustments can be made during the trial. Data are collected by structured observations, semi-structured interviews, and focus groups. Data are coded and analyzed using software specifically designed for qualitative data.

11.6 Quantitative Data Methods and Analysis

Quantitative data are collected at baseline, during the intervention, and at end of study. These data are used to test the primary outcome and analyze secondary aims and objectives. Descriptive statistics (mean, standard deviation, percentiles), frequencies, tabulations, plots, graphics, and effect sizes are produced. Cluster level as well as individual level characteristics are presented. Comparisons are made between those students recruited in 6th grade still present in the cohort in 8th grade versus those who are no longer in the cohort in 8th grade, and between those students in the 8th grade cohort versus students newly enrolled in 8th grade for end of study data collection.

Methods of analysis account for the structure of the cluster design trial, with measures of variance both between cluster (school) and within cluster (between students within the same school) [Murray 1998; Donner and Klar 2000]. Odds ratios and 95% confidence intervals are obtained from generalized estimating equation (GEE) models to analyze differences between intervention and control schools. GEE provides a method for analyzing data when the responses are correlated. The responses can be continuous, discrete, or count data. The clustering of observations within schools is

taken into account by fitting a random effects parameter for school. Correlation between all interschool observations is taken into account by the selection of covariance structure. GEE models allow for fixed (e.g., gender, race) and time-varying covariates (e.g., Tanner stage, waist), as well as adjustment for individual-level and cluster-level covariates (e.g., baseline values). Interaction terms may be included. These methods apply to analysis of point-in-time as well as longitudinal measures from a cross-sectional or cohort sample, respectively.

The primary analysis is performed on the cohort enrolled in 6th grade and measured at end of study in 8th grade. Students in the cohort provide both consent and assent and data to determine the primary outcome, BMI percentile, i.e., valid measurements of height and weight, gender, and age. Students diagnosed with diabetes at baseline are not eligible for the cohort. Intent-to-treat principles are applied as described above. Baseline value is included in the model as a covariate. Both unweighted and weighted methods of analysis are applied to evaluate consistency and interpretation of findings. A secondary cross-sectional analysis of the outcome is performed on the entire 8th grade sample (cohort plus end of study recruits).

12 STUDY ADMINISTRATION

12.1 Organization

The major organizational components and their responsibilities are described:

- The *Prevention Study Group* is composed of investigators and study staff from the seven prevention field centers, the coordinating center, the NIDDK project office, the study chair, and designated experts. The committee is responsible for the design and conduct of the primary prevention study and its pilot components.
- The *Prevention Steering Committee* is the voting body of the Prevention Protocol Committee. Members are the principal investigators of the 7 prevention field centers and the coordinating center, the NIDDK project office, the STOPP-T2D Study chair, and designated experts.
- The *NIDDK project office* participates in all decision-making activities and selects and oversees the activities of the Data Safety Monitoring Board.
- The *field centers* are located at Baylor College of Medicine, Oregon Health & Science University, Temple University, University of California at Irvine, University of North Carolina at Chapel Hill, University of Pittsburgh, and University of Texas Health Science Center at San Antonio. They are responsible for recruiting schools and study participants and implementing the protocol.
- The *coordinating center* is located at the George Washington University Biostatistics Center with responsibility for coordinating all aspects of the study, including production and distribution of materials and documents, development and conduct of study staff training sessions, development and administration of the data management system, maintenance of the central database, data analysis, and report of results in collaboration with the other investigators.
- The *Data Safety Monitoring Board (DSMB)* is composed of outside experts in the design and conduct of clinical and cluster design trials, in pediatrics, in behavior modification, and in type 2 diabetes. The board is responsible for reviewing the study documents, monitoring study progress, and monitoring participant safety.
- *Working committees* are responsible for designing and developing the intervention, administering the intervention, overseeing protocol implementation and safety, and performing collaborative activities. Committee membership is representative of the study group.
- *Central labs and resources* include the Central Blood Laboratory (Northwest Research Lipid Laboratory, Seattle WA), Communications Core (Planit, Baltimore MD), and Qualitative Data Core (University of North Carolina, Chapel Hill NC).

12.2 Study Website

The coordinating center maintains the study website, which is a secure site requiring a user ID and password combination for access. The web server utilizes the Secure Socket Layer (SSL) protocol which encrypts all traffic to and from the server. Investigators, coordinators, consultants, and other study staff who would benefit from access to the information on the website are each given a unique user ID and password which identifies the user to the web server and can be used to restrict access to particular web pages if desired.

The website contains access to study documents and information such as the protocol, manual of procedures, forms, materials, workbooks, study calendar, directory, meeting and conference call information, links to other sites, tracking reports, policies, minutes and agendas, publications status and preparation. The website is also used to enter, download, and transfer study data.

12.3 Policies

The study group has adopted three policies.

12.3.1 Conflict of Interest

The Prevention Steering Committee investigators have adopted a conflict of interest policy similar to that used by other NIDDK collaborative groups. On an annual basis or whenever there is a significant change in status, study collaborators are required to disclose any financial or related interest that could present an actual conflict of interest or be perceived to present a conflict of interest. Disclosure is required to protect each individual's reputation and career from potentially embarrassing or harmful allegations of inappropriate behavior, and to protect the integrity of study research. Forms are kept on file at the coordinating center.

The Ethics Committee determines (1) if the disclosed interests could directly and significantly affect the performance of study responsibilities and (2) the management, reduction, or elimination of the conflict. In addition to complying with the conflict of interest policies, collaborators must certify to the Ethics Committee that they have complied with all of their local and institutional requirements regarding conflict of interest and disclosure. This is accomplished by supplying the coordinating center with copies of the local IRB letter of approval and stamped informed consent form(s).

12.3.2 Publications and Presentations

The Prevention Steering Committee investigators have adopted a policy similar to those used by other NIDDK collaborative groups. The policy is administered by the Prevention Publications and Presentations Committee with approval from the Prevention Steering Committee. The policy includes guidelines for authorship, submission and review of proposed publications and presentations, ownership of the data, and setting priorities for coordinating center statisticians.

12.3.3 Ancillary Studies

According to the Prevention Study Group Ancillary Studies Policy, an ancillary study is defined as research using study participants (including their laboratory specimens or tests) to collect or derive supplemental data for purposes above and beyond those set forth in the protocol. Ancillary studies are evaluated with careful consideration of their potential impact on the objectives and performance of the primary prevention trial. Investigators and participants are entitled to prior assurance that all ancillary studies are of high scientific merit and that no ancillary study will:

- cause a deviation from the protocol,
- confound interpretation of study results,

- adversely affect participant cooperation,
- jeopardize the public image of the study,
- create a significant diversion of resources at the field centers, at the coordinating center, or at any other level,
- in any way negatively influence the cooperative spirit of the collaborating investigators, or
- otherwise compromise the scientific integrity of the study.

The policy spells out steps to propose, review, and approve ancillary studies. No field center is required to participate in an ancillary study.

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14 APPENDIX

14.1 List of Abbreviations

BMI	Body Mass Index
CBI	Computer Based Intervention
CBL	Central Blood Laboratory
CVD	Cardiovascular Disease
DAC	Dietary Assessment Center
DPP	Diabetes Prevention Program
DSMB	Data Safety Monitoring Board
FFQ	Food Frequency Questionnaire
FLASH	Fun Learning Activities for Student Health
FLOW	Fitness Laboratory on Wheels
FS	Food Service
FWA	Federal Wide Assurance
GEE	Generalized Estimating Equations
HAT	Health Action Team
HDL	High Density Lipoproteins
HPC	Health Promotion Coordinator
HPCA	Health Promotion Coordinator Assistant
HUI	Health Utilities Index
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
IRB	Institutional Review Board
LDL	Low Density Lipoproteins
20-MST	20-Meter Shuttle Test
MVPA	Moderate-to-Vigorous Physical Activity
NIDDK	National Institute of Diabetes & Digestive & Kidney Diseases
NIH	National Institutes of Health
NSLP	National School Lunch Program
OGTT	Oral Glucose Tolerance Test
PAC	Physical Activity Coordinator
PDA	Personal Digital Assistant
PDPAR	Previous Day Physical Activity Recall
PDS	Pubertal Development Scale
PE	Physical Education
PWC	Physical Work Capacity

QALY(S)	Quality-Adjusted Life Year(S)
Q/A	Question and Answer
QDC	Qualitative Data Core
RA	Research Assistant
RD	Research Dietitian
SAPAC	Self-Administered Physical Activity Checklist
SBP	School Breakfast Program
SSL	Secure Socket Layer
STOPP–T2D	Studies to Treat Or Prevent Pediatric Type 2 Diabetes
TEE	Total Energy Expenditure
TV	Television
T2D	Type 2 Diabetes
USDA	United States Department of Agriculture
USDHHS	United States Department of Health and Human Services

14.2 Previous Prevention Study Group Research Activities

The current protocol represents the culmination of a series of pilot and feasibility studies conducted by the Prevention Study Group in preparation for the primary prevention trial. To ensure a robust intervention for the primary prevention trial, the study group has conducted the following pilot studies of the various intervention components separately and in combination:

Study	**OGTT Feasibility Study**
Schedule	Winter 2003
Sample	8th graders in 12 schools, 4 at each of 3 field centers (Baylor, UCI, and UNC)
Primary Purpose	(1) Assess the feasibility of collecting measurements, including a 2-hour oral glucose tolerance test (OGTT), in the middle school setting. (2) Determine the prevalence of pre-diabetes and type 2 diabetes among 8th grade school children.
Data Collected	• Health screening including age; race/ethnicity; anthropometrics (body mass index, waist circumference, triceps and subscapular skinfolds); blood pressure; fasting insulin, glucose, proinsulin, lipids, HbA1c, and C-peptide; 2 hour post glucose load insulin, glucose, and C-peptide; presence of acanthosis nigricans; prescription medications; and pubertal status. • Family history, medical history, and demographic characteristics provided by parent/guardian. • Process evaluation including documentation of recruitment efforts and post study focus groups and interviews with students and parents to gauge reaction.
Primary Findings	The study demonstrated that a representative sample of 8th grade students participated in a health screening (representative in terms of gender, race/ethnicity, and proportion with BMI ≥ 85th percentile). Further, high participation in a school based diabetes screening was feasible (55% overall). Students, parents, teachers, and administrators appeared highly interested in obesity and diabetes and in participating in the assessment procedures. The data also indicated a significant presence of three risk factors for type 2

	diabetes: 49% of the sample had BMI percentile ≥ 85, 40.5% had fasting glucose ≥ 100 mg/dl, and 36.3% had fasting insulin ≥ 30 uU/ml. Few children (<1%) were found to have undiagnosed type 2 diabetes, suggesting that changes in diabetes prevalence could not serve as a main outcome for the trial.

Study	**Physical Education Intervention Pilot Study**
Schedule	Fall 2003
Sample	6th and 7th graders in 6 schools, 2 from each of 3 sites (Baylor, UCI, and UNC)
Primary Purpose	Evaluate the ability of the 8-week PE class intervention to engage students in activity and attain targeted levels of moderate-to-vigorous physical activity (MVPA), defined as heart rate ≥ 140 beats per minute measured by heart rate monitor. The intervention consisted of study-provided lesson plans and equipment, a 16-hour PE teacher training, a teaching assistant at each school, and a physical activity coordinator at each field center to coordinate implementation.
Data Collected	• Heart rate during PE class. • In-class observation of student activity. • Post-class student self-survey of reaction to class activities. • Process evaluation post-study interviews with PE teachers, school and study staff.
Primary Findings	About 45% of classes achieved the target amount of MVPA. Children enjoyed being active. Repetitive activities bored students, while increasing activity levels was associated with a perceived reduction in discipline problems. Formative research interviews and focus groups with school principals and PE teachers indicated a willingness to adopt lesson plans with a greater emphasis on MVPA as well as the need to create a program with enough flexibility to account for differences in PE programs across schools.

Study	**Nutrition Intervention Pilot Study**
Schedule	Winter 2004
Sample	food service areas in 6 schools, 2 from each of 3 sites (Baylor, UCI, and UNC)
Primary Purpose	Evaluate the feasibility of a 6-week intervention to implement 13 specific alterations to nutrition activities and services in middle school food services in order to provide greater availability of healthier food options in the National School Lunch Program (NSLP) meal, snack bar/a la carte foods, and vending areas. The intervention consisted of training, monitoring, and technical support provided by an experienced research dietitian to food service administrators and workers.
Data Collected	• Inventory, production, and sales data • NSLP participation rates. • Additional hours of labor used.

	• Process evaluation observation and interviews both during the intervention and post study.
Primary Findings	Most of the food service changes to the NSLP meal and snack bar/a la carte foods were successfully implemented. Of the 6 schools, 5 attained the objective of at least 75% (10 out of 13) goals and the other attained 70%. Changes related to vending machines were more difficult because vending machines were not necessarily under the control of the school food service.

Study	**Integrated Pilot Study**
Schedule	Fall 2004
Sample	6th graders in 7 schools (1 per field center)
Primary Purpose	Test ability to implement and integrate an 8-week multi-component intervention of changes to the PE class and the school food service, enhanced by a school-wide communications campaign of activities, education, and promotion. The PE component expanded personnel training and developed individual lessons into unit plans to allow PE teachers to more easily incorporate MVPA activities into their classes. The nutrition component adjusted and added school nutrition goals targeting high fiber to goals for water, sweetened beverages, fruits and vegetables, and fat content in meals and snacks. A school-based Health Action Team assisted in the delivery of educational and promotional messages and events.
Data Collected	• Student gender, age, race/ethnicity, height and weight, pre and post fitness, activity level (accelerometry), self-report sedentary behaviors, food and nutrient intake (24-hour dietary recall), psychosocial behaviors (self-efficacy, intrinsic motivation, norms), and end of study aided and unaided recall. • PE in-class observation of student and teacher. • Food service inventory and production records. • Academic performance by school-wide standardized test scores, attendance, and comportment. • Process evaluation of dose, reach, and fidelity by staff survey, focus group, and interview.
Primary Findings	Overall 62% of 6th grade students enrolled in the study. The nutrition intervention met its objective of food service goal attainment. For the PE intervention, 57% of students who wore heart rate monitors in PE class attained average heart rate ≥ 140 bpm, 35% of the time the recorded students spent at least half of the class period in MVPA, and there was a slight improvement in fitness from baseline to 8 weeks. The study name was recalled unaided by 79% of students interviewed, however recall of study messages was poor. Health Action Teams implemented from 3 to 6 activities.

Study	**Behavior Intervention Pilot Study**
Schedule	Fall 2005

Sample	6th graders in 7 schools (1 per field center)
Primary Purpose	Evaluate ability to implement the core components of a behavioral intervention—i.e., brief classroom activities, individual/group behavior change initiatives, and family outreach—and establish their feasibility and acceptability to stakeholders including youth, families, and school faculty and staff.
Data Collected	• Student gender, age, race/ethnicity, height and weight, self-report health related quality of life, peer network survey, and end of study aided and unaided recall. • Food service orders and sales of water and sweetened beverages. • Process evaluation of dose, reach, and fidelity by staff survey, focus group, and interview.
Primary Findings	*(Not available at this time.)*

Study	**PE Intervention Pilot Study**
Schedule	Fall 2005
Sample	1-2 PE teachers and 7th-8th grade PE classes in 7 schools (1 per field center)
Primary Purpose	• To study the use of techniques to improve the skills of the physical activity coordinator to work with the local physical education (PE) teacher, including ongoing training and motivational strategies to get buy-in and compliance. • To implement and test the feasibility of the new units of instruction with 7th and 8th grade students.
Data Collected	In-class observation, survey, and interview data.
Primary Findings	*(Not available at this time.)*

In addition, formative research has been conducted to inform the design and development of the intervention components. Data have been collected in focus groups and interviews from students, parents, and school staff and faculty.