Stanford
GOALS

Phase 2 Protocol

March 13, 2012

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1. EXECUTIVE SUMMARY

Stanford Goals is a large-scale, community-based randomized controlled trial of an innovative, interdisciplinary, multi-component, multi-level, multi-setting approach to treating overweight and obese children. The intervention model was designed to overcome the major barriers to success from standard clinical and research treatment models. Our novel treatment model is…

- **Innovative**, drawn from past successes and avoiding the pitfalls of past failures, and taking advantage of recent advances in our knowledge of biological and physiological, psychological, social, and environmental influences on eating, activity, sedentary behavior, and energy balance.
- **Multi-component**, targeting eating behaviors, physical activity, inactivity, and screen time, in multiple ways in multiple settings.
- **Multi-level**, intervening with individual children, families, groups, primary care providers, community youth-serving organizations.
- **Multi-setting**, intervening in primary care clinics, community centers, and homes.
- **Generalizable to real world communities and populations**, by using infrastructure and resources that already exist in many communities, and conducting the intervention in an ethnically- and socioeconomically-diverse population at increased risk for obesity and obesity-related morbidity and mortality.

The interdisciplinary and collaborative team of investigators have a track record of conducting high-quality, transdisciplinary research in childhood obesity prevention and treatment germane to clinical practice, community programs, and public policy.

The intervention will be evaluated with a two-arm, parallel group, randomized controlled trial. 240 families with overweight and obese 7-11 year old children (BMI ≥ 85th percentile) will be recruited through primary care pediatric clinics, community centers, schools, other organizations serving low-income, ethnically-diverse patient populations, and other community sites in East Palo Alto, Menlo Park, and Redwood City, California. After completing baseline assessments and enrolling in the study, families will be randomized to either an enhanced standard but state-of-the-art clinical and community health education program (the standard care health education control group), or to our integrated, multi-component, multi-level, multi-setting (MMM) intervention. The experimental MMM intervention includes:

• a theory-based community center team sports program designed specifically for overweight and obese children,

• a home-based family intervention to reduce screen time, alter the home food/eating environment, and promote self-regulatory skills for eating and activity behavior change, and

• a primary care provider behavioral counseling intervention linked to the community and home interventions.

Both the MMM intervention and the enhanced health education intervention will last for 36 months, and all participants will complete assessments at baseline, 12 months, 24 months and 36 months. The primary outcome measure is change in BMI over the entire course of the 36-month interventions.

Primary Research Question: Will a 3-year, innovative, interdisciplinary, multi-component, multi-level, multi-setting (MMM) community-based intervention to treat overweight and obese children significantly reduce BMI compared to a standard care/health education active placebo control intervention?

Primary Hypothesis: Compared to standard care/health education controls, children randomized to our multi-component, multi-level, multi-setting (MMM) intervention will have a significantly attenuated body mass index trajectory.

Secondary Hypotheses: Compared to standard care/health education controls, children randomized to our multi-component, multi-level, multi-setting (MMM) intervention will have significantly greater trajectories of physical activity (objectively measured by accelerometers) and HDL-C, and significantly attenuated trajectories of waist circumference, triceps skinfold thickness, resting systolic and diastolic blood pressures, resting heart rate, fasting Total Cholesterol, LDL-C, TG, Insulin, hemoglobin A1c, hsCRP, ALT, screen time and other sedentary behaviors, average total dietary energy intake, weight concerns, and depressive symptoms.

2. SPECIFIC AIMS AND OBJECTIVES FOR MAIN TRIAL

We propose an innovative, interdisciplinary, multi-component, multi-level, multi-setting approach to treating overweight and obese children (BMI > 85th percentile on the 2000 CDC standards). We designed this treatment model through a process of community based participatory research (CBPR) combined with past research findings and Phase 1 pilot and feasibility studies, to overcome the major barriers to success from standard clinical and research treatment models. In addition, by building upon existing resources in the community to provide an integrated treatment model, it is more generalizable to real world communities and populations. As a result, this research can be applied more broadly to improve children's health by reducing obesity-related morbidity and mortality. Our novel treatment model is…

- **Innovative**, drawn from past successes and avoiding the pitfalls of past failures, and taking advantage of recent advances in our knowledge of biological and physiological, psychological, social, and environmental influences on eating, activity, sedentary behavior, and energy balance.
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- **Multi-level**, intervening with individual children, families, groups, primary care providers, community youth-serving organizations.
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- **Generalizable to real world communities and populations**, by using infrastructure and resources that already exist in many communities, and conducting the intervention in ethnically- and socioeconomically-diverse population at increased risk for obesity and obesity-related morbidity and mortality.

To accomplish this, we have assembled an interdisciplinary, collaborative research team with a track record of conducting high-quality, transdisciplinary research in childhood obesity prevention and treatment germane to clinical practice, community programs, and public policy. Including expertise in childhood obesity prevention and treatment research, pediatric obesity clinical management, primary care pediatrics, nutrition, physical activity and exercise physiology, pediatric endocrinology, child growth and physiology and glucose metabolism, clinical psychology and behavior modification, social psychology and motivation, anthropology, neuroscience, decision-making and behavioral economics, genetics, economics and cost-effectiveness, epidemiology and statistics, public health, and public policy. In addition to being highly qualified to conduct the proposed research, our team is also experienced in collaborating with community partners and policymakers to translate successful interventions into real world practice. A further institutional strength is the Stanford University and Lucile Packard Children's Hospital's Center for Healthy Weight, which ties together all the clinical programs, research, professional education, community programs and advocacy related to childhood obesity. Therefore, Stanford represents a particularly strong environment for the proposed research, and our breadth and depth is able to contribute substantial added value to the multi-site consortium formed under this U01 Cooperative Agreement.

We will evaluate our intervention with a two-arm, parallel group, randomized controlled trial. 240 families with overweight and obese 7-11 year old children (BMI ≥ 85th percentile) will be recruited through primary care pediatric clinics, community centers, schools, other organizations serving low-income, ethnically-diverse patient populations, and other community sites in East Palo Alto, Menlo Park, and Redwood City, California. After completing baseline assessments and enrolling in the study, families will be randomized to either an enhanced standard but state-of-the-art clinical and community health education program (the standard care health education control group), or to our

integrated, multi-component, multi-level, multi-setting (MMM) intervention (the MMM intervention group). The experimental MMM intervention is based on successful past research, is designed to overcome barriers to existing treatment models, and is being finalized during the ongoing formative research phase of the trial (Phase 1). Through ongoing community based participatory research (CBPR), involving collaborations with community leaders, health professionals, our partner youth-serving community organizations, and overweight children and their families, we identified childhood obesity and risk of future diabetes as these communities' highest priority health concerns. They requested better linkages between medical providers and community programs/resources, direct help for parents/families to improve children's behaviors in the home, and greater availability of community-based programs to provide a safe place for children after school and to enhance both children's health, social development and academic achievement. As a result, our multi-component, multi-level, multi-setting (MMM) intervention includes the following integrated components:

• a theory-based community center team sports program designed specifically for overweight & obese children,

• a home-based family intervention to reduce screen time, alter the home food/eating environment, and promote self-regulatory skills for eating and activity behavior change, and

• a primary care provider behavioral counseling intervention linked to the community and home interventions.

Both the MMM intervention and the enhanced health education intervention will last for 36 months, and all participants will complete assessments at baseline, 12 months, 24 months and 36 months. The primary outcome measure is change in BMI over the entire course of the 36-month study. Secondary outcome measures include change in BMI from baseline to 12 and 24 months, and change from baseline to 12, 24 and 36 months in waist circumference, triceps skinfold thickness, resting systolic and diastolic blood pressures, resting heart rate, fasting total cholesterol (TC), LDL-cholesterol (LDL-C), HDL-Cholesterol (HDL-C), Triglycerides (TG), Glucose, Insulin, Hemoglobin A1c, high-sensitivity C-Reactive Protein (hsCRP), Alanine Aminotransferase (ALT), physical activity (assessed with accelerometers), screen time and other sedentary behaviors, dietary energy intake, percent of dietary energy intake from fat, weight concerns, and depressive symptoms. Blood and saliva will be collected for genetic material to identify hereditary moderators of intervention responsiveness. We will compare the MMM intervention and standard care control groups by computing a trajectory of change (slope) for each participant to take full advantage of all longitudinal data. Primary outcome analysis will follow intention-to-treat principles.

Primary Research Question: Will a 3-year, innovative, interdisciplinary, multi-component, multi-level, multi-setting (MMM) community-based intervention to treat overweight and obese children significantly reduce BMI compared to a standard care/health education active placebo control intervention?

Primary Hypothesis: Compared to standard care/health education controls, children randomized to our multi-component, multi-level, multi-setting (MMM) intervention will have a significantly attenuated body mass index trajectory.

Secondary Hypotheses: Compared to standard care/health education controls, children randomized to our multi-component, multi-level, multi-setting (MMM) intervention will have significantly greater trajectories of physical activity (objectively measured by accelerometers) and HDL-C, and significantly attenuated trajectories of waist circumference, triceps skinfold thickness, resting systolic and diastolic blood pressures, resting heart rate, fasting Total Cholesterol, LDL-C, TG, Insulin, hemoglobin A1c, hsCRP, ALT, screen time and other sedentary behaviors, average total dietary energy intake, weight concerns, and depressive symptoms.

Exploratory Research Questions: To help appropriately inform future research public policy and define the groups to whom the MMM intervention is best suited, we will explore the question: how do baseline biological, psychological, social and environmental variables help define the subgroups of the population that are more or less responsive to the intervention (moderators)? To help understand the mechanisms by which the intervention produces change we will explore the question: how do changes in potential mediating variables explain the outcome changes? And to better inform public policy we will explore the question: what is the cost-effectiveness of the intervention?

3. BACKGROUND AND RATIONALE

Existing clinical childhood obesity treatment programs are expensive and time-consuming to implement, able to serve only limited numbers of children, not available in all communities, often inconvenient for children and families to attend, and generally produce only modest outcomes.[1, 2] It also has been our experience, having delivered both clinic-based and community-based behavioral pediatric weight control programs for more than a decade, that group or individual behavioral counseling is avoided by many families, even when made available. As the prevalence of childhood overweight and obesity has grown, innovative feasible, accessible, acceptable, affordable, and effective weight control programs are greatly needed. Thus, we propose an entirely new model for treating overweight and obese children.

To overcome the shortcomings of existing approaches, we propose to link care provided in the traditional medical setting to community resources, to deliver the bulk of treatment in the settings where children already live and play. We will also simultaneously target multiple influences on eating, activity and sedentary behaviors at multiple levels and in multiple settings. This novel, multi-component, multi-level, multi-setting (MMM) treatment model has been designed based on the existing research knowledge base, our extensive experience performing childhood obesity prevention and treatment research and delivering pediatric care to overweight and obese children, and through input from an ongoing process of community based participatory research (CBPR) in our local communities.

3.1. Community-Based Team Sports to Increase Moderate-to-Vigorous Physical Activity Plus Reduce Opportunities for Sedentary Behavior and Snacking.

One component of our MMM treatment model is a community-based team sports program designed specifically for overweight and obese children. *Why team sports?* Team sports afford opportunities for physical, psychological and social benefits. First, team sports can provide opportunities for regular and sustained moderate-to-vigorous physical activity. In addition, an organized after school team sports program may also address neighborhood safety concerns that may keep children indoors. Families living in unsafe areas may keep their children indoors after school, potentially leading to increased ”screen time” and snacking. Participating on a team offers safe, supervised physical activity on a regular basis. Playing sports, being part of a team, wearing uniforms and team colors, receiving mentoring, modeling, and friendship from young adult coaches and opportunities to demonstrate skills in front of friends and family, may all be fun for children and thus highly motivating.[3, 4] When provided in a supportive environment including only other overweight children, these characteristics make team sports a highly attractive physical activity opportunity.

Children involved in team sports are more physically fit than their uninvolved peers and have greater involvement in physical activity over time.[5-7] For example, a prospective study of inner-city 4th and 5th grade children found that participating in school teams prevented a decline in physical activity in both boys and girls.[6] A retrospective study of low-income African-American and Caucasian women found that a history of organized sport participation in childhood predicted lower adult BMI and higher adult activity levels.[5] Unfortunately, overweight children are less likely to participate in team sports and physical activity outside of Physical Education, compared with their normal weight peers.

Our clinical and research experiences have confirmed these findings. When we surveyed a sample of overweight 8-16 year olds at a low-income public medical clinic in East Palo Alto, CA about team sports participation, in the early stages of preparation for this research, all but one of the children reported they were not involved in team sports. When asked “why?” many of the responses included poor confidence in ability (e.g., not wanting to be the slowest kid on the team or the last one

picked). When asked if they would be interested in playing on a sports team just for overweight children, all of them said they would join. Based on those interviews and our clinical and research experience with overweight children, we postulated that overweight children who were given an opportunity to participate in team sports with other overweight children would be more likely to participate in regular physical activity, resulting in increased total daily physical activity and decreased BMI. We also postulated that as overweight children improved their sports skills and confidence, they would be more likely to integrate other types of physical activity into their lives. The results of a feasibility study and a 6-month pilot randomized controlled trial strongly supported our hypotheses and the rationale for the present proposal.[8] Children who were initially reluctant to participate in a team sports program, participated at high rates, increased their levels of physical activity, decreased their BMI-z compared to controls, and many went on to join existing sports teams at their schools.

3-month Feasibility Study of Team Sports for Overweight and Obese Children. Based on a highly successful initial 9-week feasibility study, we received funding from the CDC for a longer feasibility study and pilot RCT. The soccer program was offered 3 days per week. Sessions were approximately 2.25 hours in length and started with a 1-hour homework period, followed by 75 minutes of activity. We collaborated with the Positive Coaching Alliance (also a community collaborator on this current study) to structure practices to promote positive experiences through sport with an emphasis on respect for self and others, inclusion and teamwork. Shin guards, uniforms and water bottles were provided to each player. We trained Stanford University undergraduate students as volunteer coaches and homework tutors. Thirteen children were enrolled in the 3-month feasibility trial. 9 of 13 children (69%) had never previously been on a sports team. None were currently playing sports. 11 of 13 children (85%) completed the full 3-month study. Mean ± SD attendance for children who completed the study was 57 ± 26% (range 9-89%) of possible days. Change in BMI z-scores over 3 months was 0.00 ± 0.06 (45% of children who completed the study had reduced BMI z-scores). Change in self-esteem was 0.82 ±4.05 (54% had improved self-esteem). Change in depressive symptoms was -0.27 ±2.80 (45% had reduced depressive symptoms). Change in weight concerns was -5.45 ±16.35 (45% had decreased weight concerns). Although the feasibility trial participants were not eligible for the subsequent pilot RCT (see below), they were allowed to continue to attend the soccer program along with the RCT participants randomized to team sports. 8 of 11 (73%) of children who completed the feasibility study continued with the sports program (range 6 weeks-10 months). Responses to the feasibility study soccer program from children and parents were very positive.

6-Month Pilot Randomized Controlled Trial.[8] Twenty-one fourth and fifth grade children were enrolled and randomized in the six-month pilot RCT: 9 to after school soccer and 12 to an active placebo control health education program. The mean ± SD age of children was 9.50 ± 0.58 years for the soccer group and 10.34 ± 0.84 for the health education group. Two children in the soccer group had BMI 85th – 94th percentile and 7 had BMI ≥ 95th percentile. All 12 children in the health education group had BMI ≥ 95th percentile. 6 of 9 families in the soccer group (67%) and 9 of 12 families in the health education group (75%) had total household incomes less than $40,000. 6 of 9 families in the soccer group (67%) and 7 of 12 families in the health education group (58%) had highest parent/caregiver level of education of high school graduate or below. There were 8 Hispanic/Latino and 1 Black or African-American child in the soccer group and 10 Hispanic/Latino, 1 Black or African-American and 1 Native Hawaiian or other Pacific Islander in the health education group.

Soccer was increased to 4 days per week at the request of participating children and parents. To further involve families in both the treatment and active control intervention, we also held periodic child-parent-coach soccer games and health education events. At the conclusion of both the soccer and health education programs, children received certificates of accomplishment and medals. 14 of

21 enrolled children (66%) had never previously participated on a sports team. Of the 9 children randomized to soccer, only 2 children had previously participated on a team, both for less than 1 month. All 21 children (100%) completed the study. Mean ± SD attendance for the soccer group was 42% ± 24 (range 14-86%) of possible days; 53% ± 24 (range 13-85%) for the first 3 months. One child with 0% attendance for the second 3 months was unable to attend due to a conflict with a required academic after school program. Attendance for the health education group was 46% ± 32 (range 3-94%) of possible days. No participants were lost to follow-up. There were no significant differences between groups at baseline. Differences between the treatment and control groups (Treatment minus Control) adjusted for baseline values are reported for 3-month and 6-month follow-up below.

	3-month differences between groups			**6-month differences between groups**		
	Adjusted T-C Difference* (95% CI)	**P Value**	**Effect Size (Cohen's d)**	**Adjusted T-C Difference* (95% CI)**	**P Value**	**Effect Size (Cohen's d)**
BMI (kg/m^2)	-.43 (-1.15, .30)	.23	-.56	-.48 (-1.46, .49)	.31	-.47
BMI Z-score†	-.07 (-.13, -.003)	.04	-.98	-.08 (-.16, -.003)	.04	-.97
Total activity 7a-10p (average counts/min)	105.74 (3.24, 208.24)	.04	1.22	44.29 (-41.65, 130.23)	.29	.61
MPA 7a-10p (mins 3000 to 5200 counts/min)	10.57 (1.42, 19.73)	.03	1.22	3.02 (-3.68, 9.72)	.36	.48
VPA 7a-10p (mins > 5200 counts/min)	4.37 (.73, 8.01)	.02	1.13	1.25 (-1.48, 3.99)	.35	.43

*Soccer minus Health Education Follow-up difference adjusted for baseline and baseline by treatment interaction by ANCOVA. †Significant baseline x treatment Z-BMI interaction ($p<.03$ at 3-Months and $p<0.04$ at 6-months).

Differences show medium to large beneficial effect sizes in BMI, BMI-Z, total daily physical activity, moderate physical activity (MPA) and vigorous physical activity (VPA) at both 3 months and 6 months follow-up, even in comparison to the rigorous control of nutrition education. Results for watching TV/screen time and depressive symptoms appeared to be trending toward benefits by 6 months. There was no evidence of differences between groups in measures of overweight concerns or self-esteem. Compared to baseline, all 9 children (100%) randomized to the soccer group and 5 of 12 children (42%) randomized to the health education group had lower BMI Z-scores at both 3 and 6 months. At 6-month follow-up, 8 of 9 children (89%) in the soccer program stated that they would like to continue to play on a soccer team. The other child reported she wished to spend more time with her family instead. Although we did not systematically measure participation in other sports teams, we heard reports that many of the children from the soccer group became involved with other teams at their schools. For example, one child assigned to soccer who had "requested randomization" to health education when enrolling in the study not only continued with the soccer program, but also joined the competitive soccer team at her school.

Like the earlier studies, child and parent responses to both the soccer and health education programs were very positive and enthusiastic. What children reported liking most about the program and playing on a sports team included: having fun, making friends, being a part of a team or club, the

coaches, and exercising or learning about health. Parents of children randomized to soccer reported that it helped their children by: improving their weight and eating habits, increasing physical activity, and increasing confidence and self-esteem. The majority of parents in both the soccer and health education groups reported that it worked well for their children to be in a program only with other overweight and obese children. Specifically, parents reported that their children felt more comfortable, confident and safe playing with children of similar weight.

3.2. Reducing Screen Time

Based on our studies and others, reducing screen time is one of the best-documented strategies to reduce weight gain in children. Children spend a substantial part of their lives in front of the television screens, averaging *about 1/3 of their waking hours*.[9] Low-income and ethnic minority children consume even more TV and other screen media than white children, and are more likely to have a TV set in their bedrooms.[10] Epidemiological studies of the associations between television viewing/screen time and childhood obesity have generally found a positive relationship.[11-31] The largest associations were reported from a 4-year longitudinal sample in which there was a dose response relationship between hours of television viewing in 1990 and both overweight in 1990 and the prior onset of overweight between 1986 and 1990. Attributable risk estimates suggested that up to 60% of overweight incidence could be linked to excess television viewing.[32]

A number of experimental studies of reducing screen time have now also demonstrated that reducing screen time, as part of interventions to increase physical activity and improve diet, can promote weight loss in obese children,[33, 34] and reduce the prevalence of obesity among middle school girls.[35] Our own randomized, controlled school-based study was the first study specifically designed to test the exclusive effects of reducing screen time for obesity prevention.[36] The intervention significantly decreased children's screen time, and decreased BMI, triceps skinfold, waist circumference and waist-to-hip ratio, compared to controls. We've also demonstrated the potential efficacy of this approach using a home-based family intervention in our Stanford GEMS studies. In our most recent screen time reduction study, in collaboration with Epstein et al in Buffalo, New York, we randomized 4-7 year old children with BMI ≥ 75th percentile for age and sex to a 2-year intervention to reduce their screen time by 50%, using an electronic television time manager (also part of this study) or to an assessments only control group.[37] Children in the screen time reduction group showed significantly greater reductions in their screen time and age- and sex-adjusted BMI compared to controls, maintained over the entire 2-year period. The results of these experimental studies, where a manipulation in screen time alone resulted in changes in body fatness, represents direct evidence that reducing screen time is a promising strategy for reducing weight gain, with an effect that is sustainable for at least 2 years. The home-based, family intervention model used in this study, the Stanford GEMS studies, and our ongoing studies, provides the basis for the home-based screen time intervention proposed.

One additional enhancement to our screen time reduction intervention in the proposed study will be a specific focus on eliminating eating while watching television and other screen media. In our population-based studies, Matheson et al have shown that elementary school children consume, on average, 17%-27% of their total daily weekday calories and 26%-32% of their total daily weekend calories while watching television.[38, 39] In our school-based trial of reducing screen time and reduced weight gain, the intervention group significantly reduced the meals eaten while watching TV.[36] In our recent study of reducing screen time among 4-7 year olds, intervention group children significantly decreased their energy intake, compared with the monitoring control group, and the change in television viewing was related to the change in energy intake but not to the change in physical activity.[37] These findings add to a growing body of research implicating effects of television on eating behavior. Food advertising is clearly one of the factors linking screen time with eating and obesity.[40, 41] However, distraction during eating may also be an important mechanism. Distractions, including

watching television, have been shown to have the potential to increase food consumption through several different mechanisms: triggering eating independent of hunger (prompting eating by the association of television viewing with eating), extending the duration of eating (eating until the show is done), and obscuring self-monitoring of eating/awareness of satiety cues.[42] Watching television may impair the development of satiety by interfering with habituation to gustatory and olfactory cues and may shift attention away from processing food and satiety cues and slow the rate of habituation to food cues and lead to additional eating after habituation has occurred.[43, 44] Of particular interest, there is evidence that eating may be more susceptible to distraction among obese than normal weight persons[45] leading to even greater overconsumption of calories while watching television or other screen media.

Finally, an intervention to reduce screen time responds to a frequently expressed need of parents. When we see families in the clinical setting (whether primary care or specialty weight clinic), when we perform focus groups with community members, and when our interventionists make home visits and phone calls, parents frequently complain about their children sitting for hours on end in front of the TV, computer or video games.

Our preliminary studies of reducing screen time and combined screen time reduction and after school physical activity interventions are summarized here:

Feasibility study of interventions to reduce children's television viewing. Our first study was an intensive small-scale feasibility trial involving 10 families with 3rd or 4th grade children.[46] The family-based intervention model first developed in that trial was the original basis for currently proposed home-based screen-time reduction intervention. Compared to baseline, children significantly reduced their hours of screen time (both TV alone and TV plus videotapes and video games) at 4 weeks (P<.01), and reduced screen time was maintained at the six-month follow-up (P<.05).

A primary care-based pilot and feasibility study in low-income African-American children. 28 low-income African-American families with 7-12 year old children in a single primary care practice, were randomized to receive counseling alone or counseling plus a Structured Encounter Form (SEF)-guided behavioral intervention including goal setting and an electronic television time manger, as part of their regular clinic visits.[47] Both groups reported similar decreases in children's screen time over the 4-week study period. The SEF-guided behavioral intervention group reported greater increases in organized physical activity (P=.004; Cohen's d = 1.13) and playing outside (P<.06; Cohen's d = .71). Changes in overall household television use and meals eaten in front of television also favored the behavioral intervention, with small to medium effect sizes (Cohen's d = 0.20 and 0.45, respectively). This study supports linking the home-based intervention with primary care counseling using SEFs as planned in the current study.

A school-based efficacy trial of reducing children's screen time to prevent obesity. This study involved third and fourth graders in two public elementary schools in a single school district in San Jose, CA.[36] One school was randomly assigned to implement a program to reduce television, videotape and video game use. The other school was an assessments-only control. The regular third and fourth grade classroom teachers in the Treatment school delivered the 18 classroom lesson intervention over five months (Stanford SMART, Student Media Awareness to Reduce Television; http:noTV.stanford.edu). Each household also received an electronic TV time manager and 42% reported they had installed it. The intervention significantly decreased children's screen time compared to controls (relative reductions of about one fourth to one third). Over the course of the school year, children in the intervention group had statistically significant and clinically significant relative decreases in BMI, triceps skinfold thickness, waist circumference, and waist-to-hip ratio changes, compared to controls. These changes were accompanied by statistically significant reductions in the number of meals eaten in front of the TV. Changes in physical fitness, high fat

food consumption and time spent in other sedentary behaviors were not significant but favored the Treatment group.

In addition to the effects of the intervention on the participating children, mothers/female guardians, fathers/males guardians and siblings and other children in the families of treatment group children also significantly reduced their television viewing compared to controls.[48] This is an important example of how the entire family's behavior and home environment can be altered via an intervention targeting children.

A home-based intervention of screen time reduction to reduce weight gain in young children. In our recent study performed in collaboration with Epstein and colleagues,[37] seventy 4-7 year old children with BMI ≥ 75th percentile for age and sex were randomized to a 2-year intervention to reduce their screen time by 50%, using an electronic television time manager, or to an assessments only control group. Like in the current trial, study staff programmed TV Allowances in the home to reduce television viewing, computer use, and associated behaviors. The mean number of hours of television viewing and computer games in the intervention group declined significantly more than the controls by six months and remained lower through 24 months ($P < .001$). A statistically significant group x time interaction was also observed for zBMI ($P < .05$), favoring the treatment group and persisting for the entire two year duration of the study.

Combining Community-Based Physical Activity with Home-Based Screen Time Reduction.

Stanford GEMS (Girls Health Enrichment Multi-site Studies) Obesity Prevention for pre-adolescent African-American girls. In addition to its relevance in content, GEMS was a U01 Cooperative Agreement funded by NHLBI and provides us with experience with this mechanism and format of a multi-center collaboration. Like the proposed consortium, GEMS included four field centers, a RCU and the NHLBI scientists, as well as a Phase 1 formative research phase, prior to the full-scale trials.

The Stanford GEMS pilot study intervention combined an after school dance intervention with a home-based intervention to reduce television, videotape and video game use. In designing and planning the intervention and assessments, focus groups and individual interviews were conducted with more than 150 8-10 year-old African American girls, their parents, and community leaders who worked directly with girls in schools and community centers. Of relevance to the current proposal, many of the girls, parents and community leaders suggested team sports as an intervention strategy (in addition to dance, the activity we ultimately chose). The major barriers for an after school program identified were: the need to have time to do homework and transportation. *We successfully addressed both of these in the team sports pilot studies and have done so in the present trial design by including a "study hall" at the beginning of each after school sports session and locating the program at community centers that are part of an existing community transportation network for children.*

12-week pilot study. We successfully recruited, enrolled and randomized 65 8-10 year-old African-American girls in 61 families/households. By recruiting in low-income areas of East Palo Alto and Oakland, CA. being visible in these communities, involving community leaders in planning, and performing all data collection in the community, we were very successful in enrolling and retaining a very low-income African-American study sample. Only one participant (1.6%) was lost-to-follow-up.The treatment intervention included five family-based lessons to reduce television, videotape and video game use and the GEMS Jewels after school dance program (emphasizing traditional African dance, step and hip-hop, and time for homework and mentoring). Dance groups were offered at three different neighborhood community centers (including one of the Boys and Girls Clubs in East Palo Alto). The after school dance classes were highly popular among the participating girls and their suggestions for improvement also helped inform the proposed team sports intervention (e.g., having more performances is analogous to having tournaments). The comparison group received an

"active placebo" intervention of state-of-the-art information-based health education. Means, sds, and adjusted group differences and 95% confidence intervals are presented in the Table below. Note: P-values are included for informational purposes only, as this pilot study was designed purely to test feasibility and was *not* powered to be able to detect differences between groups. Compared to girls in the "active-placebo" control condition, in just twelve weeks, girls in the after school dance and television reduction treatment condition showed trends toward reduced BMI, reduced waist circumference, and reduced television viewing.

	Baseline		**Post-test**			
	Treatment	**Control**	**Treatment**	**Control**	Adj. ΔT - ΔC (95% CI)	P-value
Body Mass Index (kg/m2)	20.95 ± 5.39	21.57 ± 5.26	21.45 ± 5.49	22.28 ± 5.65	-.32 (-.77, .12)	.16
Waist Circumference (cm)	71.00 ± 13.99	71.04 ±13.15	71.62 ± 14.43	72.12 ± 13.38	-.63 (-1.92, .67)	.35
Weekly TV viewing (hrs)	18.20 ± 12.72	20.67 ± 13.46	15.34 ± 11.66	21.33 ± 14.32	-4.96 (-13.39, 1.47)	.14

Stanford GEMS full-scale trial. The 12-week pilot study informed the subsequent, full-scale 2-year intervention trial.[49, 50] We successfully recruited, enrolled and randomized 284 8-10 year old African-American girls in 261 families from low-income areas of Oakland, CA. Families were randomized to either our culturally-tailored after school dance classes and home/family-based screen time reduction intervention or an information-based health education active-placebo comparison – both lasting for two full years. We encountered substantial challenges related to working in a severely economically depressed city that produced many hurdles to dance class attendance. These included changes in community center leadership or episodes of violent crime at or near the community centers that required us to change intervention sites six times over the course of the study, and an abrupt disruption of transportation services that took time to resolve. Despite these challenges, families positively rated their participation in the study and we achieved a tremendous level of participation in measures. Only 18 girls were lost to follow-up with over 92% of girls in both groups participating in at least one follow-up time point and 86% participated in the final 2-year follow-up. Fasting blood samples were obtained from 80% of girls at baseline and 81% of girls at the 2-year follow-up visit. The weakened intervention did not produce differences between groups in BMI (adjusted mean difference [95% confidence interval] = 0.04 [-.18, .27] kg/m^2 per year, P=.72). However, clinically important changes were produced on several secondary outcomes. Fasting total cholesterol (-3.49 [-5.28, -1.70] mg/dL per year, P<.001), LDL cholesterol (-3.02 [-4.74, -1.31] mg/dL per year, P=.001), incidence of hyperinsulinemia (5.9% versus 16.9%, P=.03), and depressive symptoms (-0.21 [-0.42, -0.00] per year, P<.05) all fell statistically significantly more among girls in the dance and screen time reduction intervention than health education. The dance and screen time reduction intervention also produced significantly greater effects on reducing BMI gain among the subgroup of girls who watched more television at baseline (P=.02) and those whose parents/guardians were unmarried (P<.01).

The results of the Stanford GEMS pilot study and full-scale trial demonstrate: (1) the feasibility, acceptability, and success of our methods to recruit, enroll, randomize, and retain a low-income sample of children and families, (2) the feasibility, acceptability, and success of our community-based data collection protocols, (3) additional evidence for the feasibility and attractiveness of after school community-center programs and home-based interventions as intervention strategies, and (4) evidence of the potential efficacy of after school physical activity and home-based screen time reduction for reducing weight gain among pre-adolescent children, despite the challenges we faced

in implementation. We learned a tremendous amount from these studies that can be applied to the current trial. Many of the procedures and protocols are being utilized. While we will continue to work in a low-income community, few other communities in the U.S. are as economically depressed as Oakland. East Palo Alto, Menlo Park and Redwood City have well-supported and well-led Boys and Girls Clubs and Parks and Rec programs that we are partnering with, making similar problems very unlikely and providing a more generalizable setting for translating results to other communities.

Stanford ECHALE (Expressing Culture through Healthful Activity and Lifestyle Education)

Following upon the successes of the Stanford GEMS Pilot Study, we were funded by NIDDK for the Stanford ECHALE study, a large scale RCT to test the efficacy of an after school ethnic dance class (Ballet Folklorico) and home-based family screen time reduction intervention to reduce weight gain among 7-9 year old Mexican-American girls. We have only recently completed the fieldwork for this study, including successful recruitment and randomization of 240 girls in Redwood City (also one of the communities proposed for the current trial), implementation of a two-year intervention for all families, and follow-up data collection. Impressively, more than 96% of girls completed at least one follow-up assessment and 90% completed the final 2-year follow-up measurements. Over the full two years of participation, average attendance at dance sites averaged nearly 50% across all sites. Screen time reduction visits were implemented successfully, and more than 85% of girls in the treatment group able stay under their weekly screen time budget at least 75% of the time. These results also suggest the difference between the Oakland and Redwood City communities, despite the low-income status of the Redwood City population. This study is further informing our current trial.

3.3. Home-Based Environmental Strategies to Alter Eating Behaviors

Recently, researchers have started to identify environmental factors that influence intake without requiring conscious, cognitive control -- what food marketing researcher Brian Wansink has called "mindless eating."[51] Evidence is mounting that small changes in the environment may alter food choices and reduce consumption of food, without cognitive awareness. One such environmental factor affecting eating is television, as described above. However, we have also identified two additional environmental strategies that seem most promising: (1) replacing short and wide and large volume glasses with tall and thin and smaller volume glasses, and (2) replacing larger diameter and volume plates, bowls and utensils with smaller diameter and volume plates, bowls and utensils.

Portion sizes have increased since the 1970's in association with increased obesity in the U.S.,[52, 53] and some of the greatest increases have occurred among foods consumed in the home.[53] In an extensive series of studies, Barbara Rolls and colleagues, along with other research groups, have demonstrated that adults and children consume substantially more food and total energy when served larger portions, without compensation or decline, over at least 11 days.[54-56] Wansink has demonstrated that when packages are doubled in size, consumption generally increases by 18-25% for meal-related food and 30-45% or more for many snack-related foods,[57] even when the food doesn't taste good.[58] In Children, the influence of portion size appears to first emerge during the toddler and preschool years.[59, 60] Increased intake tends to be associated with larger average bite sizes of the large portion without compensatory decreases in eating other foods at the same meal or across the rest of the day, are independent of energy density,[61] and are seen across income levels and among Latino and African-American children and their mothers.[62]

So why not just tell people to eat smaller portions? It has been suggested that three factors lead to overeating from larger portion sizes. One is the "clean your plate" effect.[63] A second is that packaging and portion sizes influence our consumption norms – large sized packages, larger plates and glasses, and larger servings all change our perception of what is a normal portion.[64] And third, larger portions lead to greater underestimation of the amount of calories consumed.[65] But no matter

what the reason, it appears that one can't overcome these biases through awareness, knowledge or education.[66] Humans, both adults and children, perform poorly at estimating the amount of food they serve and consume.[42, 67] Our own study of portion size estimation in preadolescent girls is a good example.[68] 8-12 year old African American girls (n=54) were served a weighed test meal of spaghetti, salad, bread and a drink. They were allowed to eat ad lib and plate waste was measured to calculate actual consumption. Immediately upon completing the meal (within 10 minutes) dietitians collected recalls from the girls. Percent errors ± S.D. based on absolute value differences between actual and estimated total grams of food and total energy of food consumed were 58.0% ± 102.7% and 67.8% ± 109.1%, respectively. For individual foods the absolute value errors varied from 48% ± 90% for the beverage to 222% ± 524% for bread. In addition to the large mean errors, the very large standard deviations indicated the wide variations in the (in)accuracies of the intake estimates.

So if people are not consciously aware of precisely how much they consume, how do they know how much to eat? Environmental cues to portion size are one way of signaling how much to eat. As noted by Wansink and colleagues, "It seems that people use their eyes to count calories and not their stomachs."[69] People use visual clues to help estimate the amount they eat. These may serve as cognitive shortcuts and/or visual illusions that trigger decision of how much to serve and when to stop eating.[70] Visual illusions in geometry are very well known. As early as the 1960's, Piaget and colleagues showed that children believe that taller thinner containers hold more than shorter but wider containers.[71] This bias in portion estimation of volumes is evident for adults as well as children and for glasses, bottles and cans, and has dramatic impacts on drink consumption.[70] For example, 12-17 year olds at a weight loss camp poured and drank 74% more calories of juice and soft drinks when they poured into a short wide glass than when they poured into a tall narrow glass holding the same volume, but afterward they estimated drinking significantly smaller amounts.[72] This illusion also appears to be resistant to practice and attention.[73] *These results suggest that replacing short wide glasses and cups with taller and thinner glasses and cups may result in reduced consumption of drinks.*

A similar visual illusion occurs with food and plates, bowls and spoons. The amount of bias in estimating the portion size of food depends on the relative difference between the sizes of the food and the surrounding plate/bowl/spoon. People overestimate the portion size when the food covers more of the area of the plate/bowl/spoon and they underestimate the portion size when the food covers a smaller proportional area of the plate/bowl/spoon.[70] Unfortunately, since the 1960's average household bowls and glasses have increased in size and the surface area of the average dinner plate has increased by more than a third (36%).[51] In two studies in all-you-can-eat cafeterias, both overweight children and normal weight adults were shown to unknowingly serve themselves more cereal into a larger 34 oz. bowl than a smaller 17 oz. bowl, while underestimating the amount they served themselves in the larger bowl and overestimating the amount they served into and consumed from the smaller bowl.[70] Even educated, knowledgeable nutrition experts are unable to cognitively overcome these visual illusions when serving themselves and consuming.[74] *These results suggest that people will serve themselves and consume less without being aware of it when eating from smaller plates, bowls and serving utensils.*

Will children and parents adjust their intake upward because they know they are drinking from taller glasses and eating from smaller plates and bowls? The results noted above from many different studies suggest that this will not occur. Even when people are informed that larger packaging causes people to underestimate their consumption, they still do not believe that their own estimates are biased.[75] People more readily accept the fact that others are influenced by environmental factors but deny that the same factors influence themselves.[76]

To assess the feasibility of our proposed intervention we performed a six-week pilot study among participants in one of our group obesity treatment programs. We selected five representative families (6 children) for the pilot. At the first home visit the research assistant completed an inventory of

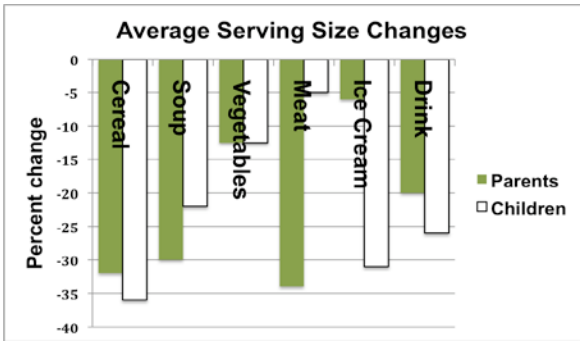
existing glasses, dishware and utensils, including measurements. We then asked parents and children to serve themselves their usual portions of cereal, soup (colored water), and ice cream (yogurt) into the bowls they typically use for those foods, using their typical serving utensils, their usual portions of meat (formed from Play-Doh) and mixed vegetables onto their typical dinner plate, and to pour a usual portion of juice (colored water) into their typical drinking glass. Then the amounts were measured with a calibrated measuring cup and/or kitchen scale.

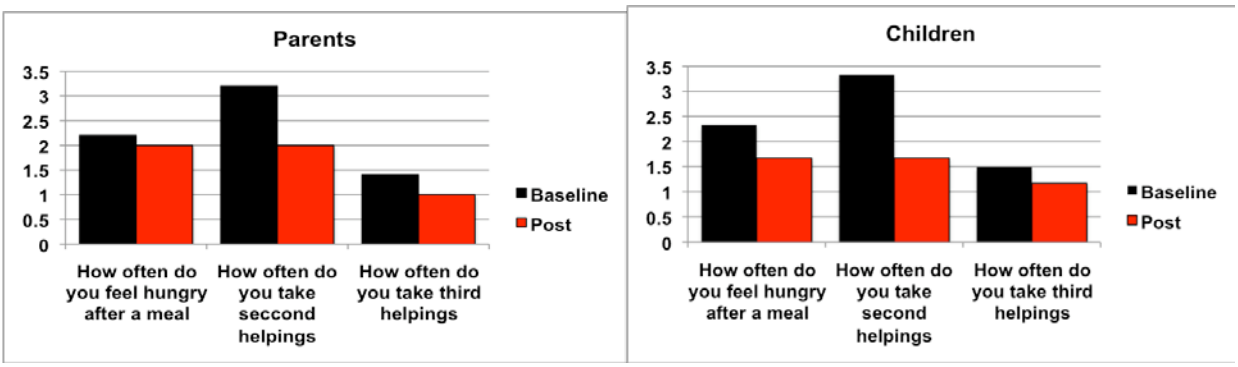
Families then chose from samples of available dishware, mugs, glasses, and utensils, to replace their current supplies. We provided a variety of styles, colors and shapes that met our size and shape criteria. We found these at IKEA, Target, Macy's, and restaurant supply stores to be immediately available. All of the families expressed excitement about getting new dishware and glassware, etc. Part of this enthusiasm seemed to stem from getting new sets of matching dishware. We found all the families had a mix of different sizes, shapes, colors and partial sets. We also found that parents tended to choose the more conservative styles and colors (usually white) while children, when given the opportunity, wanted colors or designs for the bowls and plates they would be using. Among the participating families, they never found our choices limiting nor overwhelming in variety. Three to seven days later, the research assistant delivered new dishware, etc. Only one parent objected to our removing the dishes (one father, they were a present from his parents) so we packed them into boxes to store in their own garage. All other families were happy for us to remove their dishware and store it for them. Once back at the lab, another research assistant re-measured all the dishware and found high correspondence with the in-home measures (inter-rater reliability>.97). In a prior in-home pilot study of measuring plates, bowls, mugs, glasses, serving platters and serving utensils in >30 low-income Mexican-American homes we found similar high measurement reliability (r>.95).

Across the five families in our feasibility study, comparing the sizes of the original dishware to the dishware selected, average bowl size reduced from 20.3 oz to 11.1 oz (-45%), glasses from 15.9 oz to 9.0 oz (-43%), mugs from 12.8 oz to 7.3 oz (-43%), and dinner plate diameters from 24.9 cm to 20.8 cm (16%), demonstrating the feasibility of substantially decreasing sizes.

Over the subsequent six weeks, the research assistant called families weekly to monitor their reactions to the smaller dishware and encourage their continued use. Families found it difficult to get used to for the first 1-2 weeks, especially the bowls and glasses that appeared visually much smaller to them. After about 2 weeks, however, they all reported getting used to them. Parents told us that their children easily adapted with few complaints or comments after the first week. All families said it was helping them eat less, even when they took extra helpings. No families asked for their original dishware to be returned or reported buying additional new dishware (this was confirmed at the follow-up visit, below).

After six weeks, the data collector made a final home visit. She repeated the same serving measurements as the first visit, asking parents and children to serve their usual portions using their current dishware. The results are shown in the Figure. Compared to baseline, both adults and children substantially reduced the portions they served themselves for cereal, soup, and drinks, by about 20-35% on average. Adults also substantially reduced their meat portions (-34%) and children their ice cream portions (-31%). Lesser reductions were seen in vegetable helpings on the mixed plate with meat (-12.5% for both adults and children). We were not surprised to see vegetable portions go down with all other portions, albeit not as much. Participants also reported no change or an apparent decrease in reported hunger after meals and taking second and third helpings (figures below).





Parents also were asked additional questions at follow-up about the acceptability and helpfulness of the smaller dishware. Some of their comments included: “When I wasn't at home I would still try to imagine the smaller dishes.” “Even when we assumed that we would go back for seconds, we would often forget and be done after the first serving.” “I didn't have to have so much control over what my daughter ate because she couldn't really put too much food in the dish.” “It made it so much easier…we could just pour the cereal or snacks into a bowl and know it wasn't too much.” “The bowls and the spoons helped the most because it really did take longer to eat and then I would get full.” “Rice and pasta - I definitely had to take less because of the plates.” “The dishes are cute and I got more storage space in my cupboards because they are so small.” All five families wanted to continue using their new smaller dishware. Only one family wished to keep their old dishware (only for entertaining) but the other four families did not want their original (larger) dishware back.

In sum, *this short-term pilot test demonstrated (1) the feasibility and acceptability of substituting smaller bowls, plates, mugs, glasses, and serving utensils for families participating in a weight control program, (2) the feasibility of our protocols, and (3) that smaller dishware appeared to result in serving smaller portions without evidence of increased hunger.*

In addition, we are conducting a new trial testing similar home environmental change strategies to reduce overeating and eating while watching television when added to our standard clinical family-based, group, behavioral weight control program. What we learn from that trial is directly informing our intervention design and protocols for the COPTR trial.

3.4. Family-Based Behavioral Counseling

Since the submission of the original proposal, we have added family-based behavioral counseling to our experimental intervention. This is based on (1) our experience with adding home-based environmental changes to our standard family-based, group, behavioral weight control program, and (2) our thoughts about the desirability to provide a greater variety of complementary strategies to meet family needs and styles and promote long-term changes over at least the three-year intervention period in the current study. Therefore, we have added an individual family-based version of our standard group, behavioral, pediatric weight control program. This intervention will be integrated with the home environment intervention, so does not require additional resources.

The history of obesity treatment has generally been one of relative disappointment. Most treatments for children have produced only modest, unsustained effects,[77, 78] and some have been associated with additional health risks. [79] Adult treatment results are generally even more disappointing,[80] and minority adults appear to have less success than whites.[81] A systematic review of randomized, controlled trials of lifestyle interventions for the treatment of pediatric overweight concluded that most studies were too small and that the number of studies was insufficient to compare the efficacies of various treatment approaches or components.[2] In the absence of such data, studies of treatments in research settings[77, 82] and of adult obesity[83, 84] have provided the most

useful direction.[1, 85] In children, behavior modification has generally produced losses of 5-20% of excess weight, of 1-3 BMI units, or both, over 3-6 months; changes reported over 6-12 months range from a 25% loss to a 10% increase in excess weight, a loss of 0-4 BMI units, or both. Long-term follow-up, as reported by Epstein et al, has shown increases of about 3% to decreases of about 20% in excess weight after 2-10 years.[77] These long-term beneficial outcomes are unique in the field. Epstein and colleagues, have demonstrated long-term (10-years) success in up to 30% of children in their family-based, group behavioral treatments.[82, 86] For this reason, we have designed our own clinical pediatric weight control program around their model. We have adapted their methods to be more generalizable for the diverse racial/ethnic and socioeconomic status patient population that we serve. This program serves as the basis of our individual family-based behavioral counseling intervention.

The Stanford Pediatric Weight Control Program (SPWCP) was started in 1996 by Dr. Robinson to meet an unmet clinical need for obese children and their families in the San Francisco Bay Area Mid-Peninsula and San Jose regions served by Lucile Packard Children's Hospital at Stanford. It has been systematically enhanced over the years to its current form, based on evidence, to become a state-of-the-art behavioral weight control program.[87] The program has always consisted of a family-based, group, behavioral intervention, adapted closely from Epstein's Traffic Light diet and exercise program for children[82, 88] but modified to be generalizable to the more racially/ethnically and socioeconomically diverse population that we serve.[85] We chose the Traffic Light model because it represented the most extensively studied and most efficacious model available in the literature. Dr. Epstein was of great assistance in the initial development of our program, sharing many of their materials and protocols and helping us translate their laboratory-based approaches to be more feasible in a clinic setting. We also started with the 8-12 year old age group as that is the only age group with evidence of long-term efficacy in Epstein's studies.

The First Generation Program: was a ten-week intervention with a 6-month follow-up. MediCal families (California's Medicaid) were specifically targeted in recruitment, as in all subsequent programs. Mean percent overweight at baseline was 81% (range 31% to 160% overweight). Because children are growing, we use percent overweight in this program to describe their weight relative to the norm for their sex, age and height. For example, 100% overweight is double the 50th percentile (median) BMI for a child of the same gender, age, and height. The mean change in percent overweight by the end of the ten-week intervention was -6.0% (range -19.1 to +5.8). An average reduction of 6.0% is an average reduction from 181% to 175% of the median BMI for age and sex). The mean change in percent overweight at the six-month follow-up was -4.9% (range -28.2 to +9.4). 34 of the 35 original children (97%) participated in the 6-month follow-up assessment. Therefore, dropout was minimal and, despite the limited length of the intervention, many of the children had clinically significant responses to the program.

The Second Generation Program tested the feasibility and efficacy of a longer intervention. Earlier program participants reported that 10 weeks was insufficient to instill enough confidence to maintain the behavioral changes they had made after the program stopped meeting on a regular weekly basis. In addition, since the 1960's it has been known that longer treatments generally produce greater and more lasting weight control effects among adults.[89, 90] It was likely that longer treatments would also be beneficial for treating obese children.[91] Thus, we designed a program of 6-months of weekly meetings. Three groups of 10-12 families (32 children in 31 families) completed the first 6-month program. Children were 53% white, 16% Latino, 9% Asian, 9% Pacific Islander, 6% African American, and 6% Other, and more than 20% had total household incomes < $35,000 per year. Dropout rates continued to be remarkably low with 29 of 32 children (91%) still participating at the end of the six-month program (and all three dropouts were losing weight when they dropped out). The revised, longer treatment also resulted in substantially greater weight changes. Mean percent overweight at baseline was 73% (range 31% to 135% overweight). 27 of 29 children who completed the program (93%) reduced their percent overweight and the mean change after six months was -

10.2% (range -29.5 to +7.9), about twice as much weight loss as the shorter first generation program.

Third Generation Programs: Between 1999 and 2004, we continued to enhance and expand the program, adapting it for adolescents (aged 12-15 years) and for Spanish speaking families. Although the basic structure of the program was maintained, these represented significant revisions; not just language and reading level but also social and cultural tailoring. For example, for Spanish language groups, using Mexican-American group leaders, emphasizing verbal over written information incorporating Mexican-American foods and activities, and integrating cultural values, norms, attitudes, and expectancies into the goals and strategies of the intervention – such as familism, collectivism, and religiosity. We implemented 20 groups (10 English 8-12 year olds, 8 Spanish language 8-12 year olds, and 2 Teen English groups) involving 217 children in 202 families. A remarkable 180 of 217 children (83%) in 171 families (85%) participated through the entire six months – an outstanding and unprecedented rate of retention for a clinical childhood obesity treatment program. 151 of the 180 children who completed the program (84%) reduced their percent overweight. The average ± s.d. change in overweight was -8% ± 9% (range of -38% to +16%). 198 parents were weighed at the beginning and end of the program. Of 163 parents (82%) who were overweight at the beginning (BMI ≥ 25), 120 (74%) lost weight. The average ± s.d. weight loss was 7 lbs ± 10 lbs, with a range of -47.9 to +17 lbs.

Current program: The program has existed in its current form since September 2004, implementing groups for 8-12 year olds and 13-15 year olds and in both English and Spanish. The program consists of six months of weekly sessions, delivered to groups of 10 -12 families. At each 90-minute weekly session children and parents are weighed-in and receive individual feedback from a behavior coach (group leader) about their weight and behavior changes/progress toward goals over the prior week. This occurs during the first half hour. Children and parents then split up for the next half hour, meeting in separate groups with a behavior coach, to discuss the topic of the day. Children and parents come back together into a single group for the third half hour, for a group activity to start to master the day's topic behavior and to set their goals for the following week. The first 7 weeks focus on eating behaviors. Children and parents/guardians learn the traffic light food categories to help them count and change their intake. Red = foods to reduce; yellow = the bulk of the diet and foods to eat in smaller amounts; green = very low calorie foods to consume freely, with traffic light color determined by energy density.[61, 92, 93] High energy density foods are "red light" foods. Topics emphasized during the first seven weeks are self-monitoring according to the colors with a personal behavior diary, maintaining a balanced diet and, starting in week three, setting goals to reduce red light foods, reciprocal contracting with parents/guardians, and the appropriate use of rewards to build intrinsic motivation. Session activities include modeling behavior, practice to promote enactive mastery, role-playing to overcome barriers, and social support. At the seventh session, each child and his/her parent(s) meet individually with the behavior coaches to determine whether they have mastered the skills taught in Module 1, and are ready to move on. The next seven sessions emphasize the skills presented to date, while introducing an additional focus on healthy lifestyle physical activity. Children earn "activity points" by adding lifestyle activities and can earn a pedometer to start recording steps once they achieve their first level activity goals. Choice of activity is an important motivating design feature.[33] The fourteenth session is another individual meeting with the behavior coach to review mastery of skills taught over the first 14 weeks. The final 10 sessions alternate between continued lessons in the same format (e.g., general problem solving, fast food, holidays, difficult family members, and maintenance skills) and supervised family physical activity, with parents and children learning new skills to use into their daily lives. These activity sessions were repeatedly requested by families in prior generations of the program.

Between September 2004 and December 2007, we implemented 29 groups involving 314 children/teens (13 English and 9 Spanish language 8-12 year old groups and 5 English and 2 Spanish 12-15 year old groups). The children were 62% girls and 38% boys and reported their racial/ethnic groups as 21% white, 7% African-American, 56% Latino/Hispanic, 1% Native American,

2% Asian and 13% other (including multi-ethnic). 86% of children completed the full 6 month program with an average reduction in percent overweight of -9.5% (range: -45% to +12%).

Individual family behavioral counseling. We have now developed a version of the SPWCP for use in the clinical setting with individual families over a series of twenty 30-minute sessions. This resource provides the basis of the family-based, behavioral counseling for the current trial.

3.5. Integrating Primary Care Provider Counseling with Community and Home/Family Interventions

Our experiences as primary care and subspecialty pediatricians have made us intimately aware of the limitations of traditional medical care for addressing childhood obesity. The U.S. medical care and payment system, particularly primary care pediatrics, is best suited to dealing with acute illnesses with a single cause and a single solution (e.g., antibiotics for ear infections, surgery for appendicitis). Complex, chronic, and multi-factor problems, involving multiple levels and settings of influence, such as obesity, represent a formidable challenge to the primary care provider and the standard system of care. Surveys of pediatricians and other child health professionals indicate that they rate childhood obesity as a top priority for treatment, but identify lack of time, reimbursement, children's and parents' motivation, and support services, and limited effectiveness, confidence and self-efficacy in their own skills, as barriers to addressing the problem.[94-99] Ultimately, providers are left highly frustrated with few effective tools or resources to help them.[100] This is reflected in the six-month waiting list for new patients referred to our Pediatric Weight Clinic, a multidisciplinary evaluation and management clinic at Lucile Packard Children's Hospital at Stanford. This is also consistent with our own long-held observations that the traditional medical model, and particularly primary care, are very poorly suited for obesity prevention and treatment. Therefore, instead of trying to directly combat the barriers presented by the current medical care system (most of which are far beyond our control) we acknowledge them and propose an alternative model.

In our focus groups and interviews (and many local community task force meetings) with local primary care providers, the vast majority are not interested in learning to deliver their own intensive treatment programs. Instead, they primarily request two resources: (1) simple and quick tools and guidance to help them counsel patients and families and (2) community treatment programs/health promotion resources where they can refer their patients and families. Our proposed MMM treatment model is designed to address both of these needs. First, we will provide tools to community primary care providers to help them assess patients and identify those most appropriate for referral to our study. Second, the MMM treatment model will provide them with a single mechanism for referral. Third, we will provide them with Structured Encountered Forms (SEFs) for counseling that are specifically tied to the goals of the community and home/family interventions, Structured Encountered Forms are a simple quick tools, that have been found to be particularly easy and effective for integrating new skills into practice.[101] In a prior randomized controlled trial, we used them to significantly improve provider knowledge, increase recommended behavioral screening and preventive counseling, improve quality of care, and enhance parent satisfaction of visits in primary care practices of Pediatrics residents.[101] We have also used SEFs as part of a primary care-based pilot study of reducing screen time for African-American families, described above.

Why include medical providers at all? One could propose a community-based treatment program for overweight and obese children without the involvement of the health care sector. We believe, however, including health care professionals—particularly primary care providers and clinics—can enhance the effectiveness of a community-based treatment program. As health authorities to both children and their parents, they have the access and the influence to make key recommendations on eating, physical activity, and sedentary behavior throughout children's lives. More than 75% of children see a health professional at least once every six months,[102] providing frequent opportunities to assess and counsel children and parents. As shown in our screen time study noted above, primary care provider counseling can produce behavior change.[47] While additional evidence is still

sparse for children, studies of brief dietary, physical activity, and smoking cessation counseling for adults in primary care settings have found it to be effective in changing behaviors.[103] By integrating primary care providers into the MMM treatment, it further communicates the importance of the recommended behavioral changes, putting them on par with immunizations, development and other issues addressed in the medical setting. In addition, as potentially influential and respected members of the community, health professionals also have the authority to raise concern about childhood obesity and advocate for strengthening community efforts.[103]

By shifting the emphasis for ongoing treatment to the community and home/family settings, we aim to free primary care providers from unrealistic expectations while still utilizing their strengths and interests in a way that fits within the structure of their practices. This role is also consistent with the recommendations of the recent "Expert Committee Recommendations Regarding the Prevention, Assessment, and Treatment of Child and Adolescent Overweight and Obesity."[104]

4. FORMATIVE RESEARCH-- PHASE 1

4.1. Aims, Objectives, Interventions, Measurements

The Phase 1 formative phase of the project consists of about 20 months (September 2010 through June 2012) for site-specific and consortium (common) protocol development, planning, formative research and pilot testing in preparation for the four full-scale, Phase 2 randomized controlled trials at each of the four field sites and the RCU. Phase 1 includes a very ambitious set of tasks to accomplish in a relatively short time period, but both site-specific and common elements have progressed extremely well.

The Phase 1 objectives for the consortium are to establish a functioning consortium among four field sites and their research teams, each designing and conducting their own full-scale randomized controlled trials with their own intervention approaches and a mix of site-specific and common measures, a research coordinating unit (RCU), and program scientists from NHLBI and NICHD, to develop common study elements and collaborative protocols, procedures and a common element manual of procedures (MOP). There has been tremendous progress in achieving these objectives and they are described in the RCU report. Stanford has made substantial contributions to this process.

Our primary Stanford-specific Phase 1 objectives are:

1. To design, develop and refine interventions, measures, implementation strategies and community partner relationships,
2. To pilot test key intervention components, measures and implementation strategies, and
3. To develop our Stanford protocols, procedures and manuals of operations (MOPs) for our Phase 2 randomized controlled trial.

We have made substantial progress towards achieving all of these objectives and are in an excellent position to move forward to Phase 2 starting this coming summer. It is impossible to include a comprehensive description of all of this progress to date, but some descriptions and highlights of our key findings and recommendations from Phase 1 are summarized below.

4.2. Results from Phase 1

4.2.1 Community Advisory Board and Partner Relationships

Although we had pre-existing relationships with community leaders and organizations in East Palo Alto, Menlo Park and Redwood City, one of our first tasks was to establish a Community Advisory Board of consultants for this specific project. The Community Advisory Board will help us throughout the entire life of the project, and has already provided invaluable input to our project design and implementation strategies, to insure the project is sensitive to the needs and expectations of the community we serve. Membership of the Community Advisory Board may change over time as the needs of the project change. This process has been very effective in past research, particularly for helping the study address unexpected challenges and changes in the communities over time. Our initial membership is heavily weighted toward representatives of health care clinics and community centers who will be sources of participants, as well as our community partner organizations, because of their input on the development and planning of protocols and procedures.

Neel Patel, MD	Medical Director, Fair Oaks Children's Clinic
Jose Manuel Pena, MD	Pediatrician, Willow Clinic, San Mateo County Medical Center
Wayne Easter, MD	Pediatrician, Kaiser Permanente Redwood City

Mary Giammona, MD, MPH	Medical Director, Health Plan of San Mateo
James Harris	Director of Operations, Boys & Girls Club of the Peninsula (BGCP)
Richard Washington	Unit Director, BGCP Menlo Park Clubhouse
Marcus Jackson	Athletic Director, BGCP Menlo Park Clubhouse
Debbie Bickell	Associate Executive Director, East Palo Alto YMCA
Eric Stein	Senior Associate Athletic Director, Physical Education, Recreation, & Wellness. Stanford University
Jim Thompson	Executive Director, Positive Coaching Alliance
Gladys Garcia	Program Manager, Research & Evaluation, Team Up for Youth
Anonymous (2)	Two youth who were participants in our SPORT after school team sports pilot study for overweight children from the same community (names withheld to protect confidentiality)
Anonymous (2)	Two parents of children in our age range who use public community clinics for their medical care and attend the BGCP (names withheld to protect confidentiality)

During Phase 1, we started with monthly meetings that have evolved to scheduling quarterly meetings of the Community Advisory Board, based on members' availabilities. In addition, many members of this group have made themselves available for individual and small group consultations that have often also included other members of their organizations. Many of the results of these meetings have been integrated into our design, protocols and procedures.

In addition to the Community Advisory Board, we have also continued to build relationships with the Redwood City Parks and Rec Department and School Principals and teachers in the Ravenswood and Redwood City Elementary Schools that server our neighborhoods. For our pilot study (see below) we did some recruiting from some of the elementary schools and explored use of their field space. Similarly, we decided to set up a site at an elementary school where the after school program is run by the Redwood City Department of Parks and Recreation (described below). We believe that involvement of these additional partner schools and organizations during the Phase 1 pilot will further assist in our recruiting and implementation success in Phase 2.

4.2.2 Developing and Refining Interventions

Major effort in Phase 1 has been devoted to intervention development and refinement. Our extensive past experience in successfully developing and testing behavior change interventions for children and families has taught us that a great idea is far from enough to ensure success. Every time we conduct a new study we learn a tremendous amount and new approaches rarely work the very first time they are tested. That is why we thought it important to build our innovative MMM intervention from a foundation of elements with some demonstrated preliminary feasibility and efficacy.

Although we started with interventions that already have demonstrated success in other studies and settings, we have used Phase 1 to make substantial revisions to (1) further improve the fidelity of the intervention components to more faithfully reflect the underlying theory and conceptual intervention models, and (2) ensure the relevance of the intervention framing to our target audience.

As demonstrated by our past work, described above, we have a wealth of experience developing and implementing community-based health behavior change interventions and we have developed strategies and methods for formative studies that best lead to success. We believe that a large part of our success to date is due to (1) our focus on theory in intervention design and (2) our extensive use of formative research and pilot testing to develop intervention protocols and procedures.

One of the first activities of our intervention development process was to review and explicitly define the hypothesized causal pathways underlying our intervention. We call this our "working

backwards" approach, because it involves specifying our primary objective (altering body mass index trajectory) and working backwards, step-by-step through possible causal pathways to achieve that goal, ending with our specific intervention approaches. This becomes a rather large network of boxes and arrows that serves as a blueprint for our intervention and the intermediate objectives we aim to achieve at each level. As the mechanistic underpinning for our intervention, we continue to refer back and measure our intervention against it as we design the specific elements of our intervention, a process that will continue through all of Phase 1.

The next activity was to start a theory review. Our conceptual model derived from Social Cognitive Theory (SCT) is described with the interventions descriptions. We use the key processes specified in SCT to design the macro- and micro-elements of the intervention. Throughout Phase 1 we have been reviewing the theory and how it is applied for behavior change interventions. This has involved all members of the research staff and includes reading key literature with accompanying discussions. We find this to be a very fruitful way to improve intervention design, and ensures our interventions reflect the theoretical concepts we wish to test. In an area like obesity treatment, that has been so resistant to solutions in the past, we believe it is particularly important that our interventions are true to the underlying theory, making this theory review so helpful. We will also continue this process for the balance of Phase 1, particularly once we have more results of our ongoing pilot testing.

Another innovation in this project was our behavioral science "think tank" (or "dream team," as it is referred to by Dr. Robinson) including Professors Albert Bandura (social psychology), Mark Lepper (social psychology), Carol Dweck (social psychology), Geoff Cohen (social & educational psychology), Sam McClure (neuroscience), Greg Walton (social psychology), and Ellen Markman (developmental psychology). This has been a very exciting and successful element of our formative studies. Our primary goal was been to apply innovative findings from neuroscience, behavioral economics and social, developmental, and cognitive psychology, to increase motivation, performance, and perceived self-efficacy. We have identified a number of strategies from other areas of research, primarily educational performance for disadvantaged, minority children, which we are now applying to our interventions for weight control. Many of these methods have their greatest educational and health impacts among the highest risk children. One appeal is the perceived similarities between self-stereotypes of failure and alienation experienced by disadvantaged minority students in educational settings and overweight and obese children relative to their experiences with weight control. Another is that our target population is mostly disadvantaged, ethnic minority children. The approaches we have been most excited about include, strategies from Mark Lepper's research on intrinsically motivating educational design (e.g., the seven C's of intrinsic motivation)[105]; Carol Dweck's work on implicit theories and promoting a "growth mindset"[106, 107]; Geoff Cohen's value affirmation interventions[108, 109]; Greg Walton and Geoff Cohen's social belonging interventions[110]; Greg Walton and Christopher Bryan's identity versus behavior (noun versus verb) framing[111]; Sam McClure's work on loss aversion, time discounting and preferences[112-114]; Ellen Markman's pilot work on teaching mechanistic understandings to young children (unpublished); and additional findings on choice and decision-making from neuroscience and behavioral economics, all within the conceptual explanatory model of social cognitive theory, with an emphasis on promoting agency, self-efficacy and collective efficacy.[115, 116] We have now applied these approaches to the framing of our existing interventions and have been testing them in our pilot studies. The growth mindset frame has been particularly useful for linking the different home-based and team sports intervention components with a common theme. We believe our use of these theoretical constructs represents one of the most exciting and innovative aspects of our study and will help our interventions stand out from other obesity treatment approaches in their eventual efficacy and effectiveness.

Two members of our "think tank" have an even greater and formal involvement in the project as co-investigators. Professor Lepper helps us apply the "7-C's" of intrinsic motivation, many of which he first identified and characterized, to the both the underlying structure of the interventions as well

as the framing of messages and detailed implementation strategies. Similarly, Professor McClure (also an Early Stage Investigator) helps insure that our intervention designs and implementation strategies effectively utilize heuristic biases identified in Prospect Theory and subsequent cognitive neuroscience research, such as loss aversion, time discounting, endowment bias, the effects of cognitive load on decision making, etc. These are areas of active research for Professor McClure and both he and Professor Lepper have been help us translate the results of laboratory-based studies to our real world research.

Along with "working backwards," the theory review, and our "think tank" we started Phase 1 with a large number of individual ethnographic interviews and focus groups (starting with open-ended questions, to explore general personal, community and cultural values and attitudes, and then moving on to semi-structured interviews, to evaluate specific intervention options derived from a combination of earlier interview material and theory-driven ideas). As part of this information gathering process we also used methods derived from the product design field to produce the most acceptable and effective intervention components. We collaborate with the Graduate Design Program at Stanford (commonly referred to as the d.school) on several other projects, and have adopted many of their methods (often considered the IDEO approach, for the pioneering IDEO design firm that played a key role in creating the Stanford d.school). These methods are characterized by iterative cycles of rapid prototyping of design elements with testing in small representative samples of participants, revisions or development of new prototypes, further small group trials, etc. Each cycle of prototyping and pilot testing only takes 1-2 weeks making it a very efficient way to get feedback. We also used similar approaches to test preliminary messages and activities with extremes from the sample (e.g., very high TV watchers, those who have never participated in sports, etc.) to help identify issues or new strategies that would be less obvious or slower to become evident in more general "average" samples, yet greatly informs strategies that we can apply to the entire sample. Finally, instead of only asking participants for their reactions, we rely much more heavily on direct observation of participants while they interact with prototype materials or activities. In some cases this included role playing-like activities where participants and research staff acted out parts of the intervention. Similarly, we sometimes combined direct observation during these enactments with continuous concurrent verbal reporting of "what are you thinking?" and "what are you feeling?" during the process. We focused a lot of this work on implementation aspects of our after school activities and TV reduction, but also did some of this work with primary care providers. We feel these methods helped us more rapidly and effectively make choices about how to design, frame and support different components of our interventions compared to more traditional ethnographic approaches. We are also continuing to use these methods to try out innovations and overcome barriers identified during our ongoing pilot studies.

As part of this process we are also paying particular attention to how we are applying the theoretical constructs. For example, to focus on Social Cognitive Theory's four key processes of learning a new behavior (attention, retention, motivation, and production) we focus on whether (a) the stimulus materials and methods we are developing are appropriate to engage and direct the attention of our target audience; (b) the form of the intervention (i.e., language and skill demands, information level, performance objectives) matches the cognitive and behavioral skill abilities of our target audience; (c) sufficient performance (cognitive and behavioral) opportunities are provided; and (d) whether the activities and incentives are relevant and attractive to our target audience and thus likely to serve as successful prompts for action. This method of systematically tying our formative research to our theoretical model is another way we make sure our intervention faithfully applies the underlying theory.

We should also note that we do not limit our definition of "participants" to only the children and their parents who enroll in our study. Because implementation is key to any successful behavior change intervention, we design our interventions for those who will help deliver the intervention in the real world context in which we work. Therefore, we have included siblings, grandparents and other household members, Boys and Girls Club and Parks and Rec staff, volunteer coaches, and

primary care providers and their office/clinic staff in our formative research processes. These are all key players in determining whether a very creative, theoretically sound and potentially effective intervention ever gets a chance to show its worth. We believe this also helps to maximize the potential future generalizability and disseminability of our interventions and results.

To provide a small taste of some of the types of activities we conducted during the early months of Phase 1 (in preparation for the pilot trial) we will include a list of some examples of formative research activities that we conducted.

- Exploring competing scenarios for training, implementation and QA monitoring of coaches with leaders of the Positive Coaching Alliance, the BGCP, Team Up for Youth – Coaching Corps, Scholars in PE, College Coaches, College Athletes, Coaching Corps volunteers and our own Stanford student volunteer coaches.
- Interviews with community center Athletic Directors.
- Direct observation of ongoing successful (and not so successful) after school programs with particular attention to scheduling, homework, snack use, discipline, physical activity, participant enthusiasm, attendance, "class control" type strategies, etc.
- Focus groups and questionnaires of after-school program staff in a variety of different programs and settings about motivations for participation, successful models/components of after school programs, logistics, summer programming, and weather accommodations.
- Varying approaches to recruiting and assigning student athletes for intermittent cameo appearances at after-school sessions, their roles during the sessions, and opportunities for more consistent involvement.
- Varying approaches to "field trips" to athletic events.
- Interviews, focus group and role playing with community center neighborhood advisory groups/parent groups. Particular attention to receptivity to standard care/health education intervention components.
- Hours upon hours of systematic observations of activities at after-school programs at community centers for everything from recruitment and enrollment, financial aid, registration, emergency information collection, attendance monitoring, classroom control, tutoring strategies, use of the equipment, physical space, snack logistics, coaching, implementation of sports and fitness curricula, safety procedures, first aid, rewards and punishments, uniforms and incentives, and participation, transportation, sign-ins and sign-outs, parent involvement, personal property protection, rain/cold weather contingencies, birthdays, mandatory reporting to Child Protective Services, etc., etc., etc.
- Hours upon hours of systematic direct observations in local primary care offices, clinics of primary care professionals, clinic nursing and administrative staff, and patients (e.g., use of paper and/or electronic medical records, mechanisms for handling outside lab and consultations reports, documentation strategies, communication strategies, collateral materials and programs available, opportunities for waiting room communications, etc.)
- Review of new literature on primary care interventions. Interviews of investigators doing primary care counseling interventions for obesity but also other preventive programs.
- Addition of a co-investigator with extensive experience in practice-based interventions for reading, health literacy and asthma.
- Multiple focus groups and individual and group interviews of primary care providers and front office administrators.
- Attendance at local health care community task force meetings focused on nutrition, wellness and obesity in San Mateo County.
- Small group role playing and iterative trials of Structured Encounter Forms (SEFs) and prescription pads.
- Self-experimentation of approaches and materials with investigators in their own practices/clinics.

4.2.3 Phase 1 Pilot RCT

Based on the early Phase 1 formative studies, we designed our Phase 1 Pilot trial to maximize its potential value for informing Phase 2, in the short period of time available. As a result, we targeted the pilot trial to test some key elements of our intervention and measurements. The Pilot trial is still ongoing, but it has already proven extremely useful in our development and refinement of intervention and measurement methods for Phase 2.

Recruitment and Baseline Assessments

We successfully recruited and enrolled/randomized our goal sample of 40 families (48 children) over approximately four months.

Ethnicities and races are shown in the table below for both the full sample and the analysis sample of index children.

Table 4.1. Pilot Study Sample Ethnicity and Race

	All			Analysis Sample (index children)		
	Total	Female	Male	Total	Female	Male
All, N	48	25	23	40	25	15
Hispanic/Latino	45	23	22	37	23	14
White	11	7	4	9	7	2
Black/African American	2	1	1	2	1	1
Other	34	16	18	28	16	12
Multi-Racial	1	1	0	1	1	0

To be able to test after school interventions in two different types of settings, and to further our relationships with multiple partners, we recruited from two distinct neighborhoods. We started recruiting in northern East Palo Alto and Menlo Park (closer to the Menlo Park BGCP) but after enrolling about 2/3 of our target we added recruiting in Redwood City (closer to Hoover Elementary School). We recruited from primary care clinic waiting rooms, after school programs, schools, churches and other community locations (e.g., shopping malls, laundrymats). One of our partner primary care practices also mailed information to their patients about their participation in the program. Because participants were recruited using multiple methods, and the time and number was limited, it is difficult to make definitive conclusions about the most productive recruiting strategy. However, it did appear that recruiting from after school programs may have been the most productive and recruiting from primary care waiting rooms may have been the least efficient. However, we have done some problem solving with our primary care partners to try to enhance primary care recruiting for Phase 2.

Based on our experience in Phase 1 we have lengthened our Phase 2 recruitment and enrollment/randomization interval to 18 months, more consistent with the other four COPTR studies. We believe this is being cautious but realistic because a 3-year treatment study requires motivated families who perceive their child's overweight or obesity to be a high priority problem. This reduces the number of potential participants in any geographic area, regardless of the high prevalence of obesity in our target communities.

Baseline measures: All participants (100%) completed all baseline measure prior to randomization. That included child and index parent height and weight and all other anthropometric measures, all child and index parent survey measures, all child 24 hour recalls (x3), at least four days with sufficient minutes of accelerometry, and fasting blood samples.

Table 4.2. Pilot baseline diet and accelerometry completion

	Number of dietary recalls completed			Accelerometry	
	1	2	3	6+ days	4 days
N*	48	48	48	46	2**
% of pilot sample*	100%	100%	100%	96%***	4%
% of pilot analysis sample	100%	100%	100%	97.5%	2.5%

* 48 children in 40 families
** In both cases battery shutdown limited number of days of data
*** 97.5% of pilot analysis sample

Although we know that requiring completed data prior to randomization tends to lengthen the time required for full recruitment into the study, we believe these risks are outweighed by the potential benefits to minimizing risk of loss-to-follow-up and the associated threats to both internal validity and generalizability. These results demonstrate the feasibility of requiring complete data prior to randomization in our sample.

Table 4.3. Select Baseline Index Child Characteristics (Analysis Sample, N=40)

Baseline Child Measures	N	Mean	SD
Age (yrs)	40	9.1	1.1
Height (cm)	40	136.8	6.8
Weight (kg)	40	47.1	8.7
Body Mass Index (kg/m^2)	40	25.0	3.3
Triceps Skinfold (mm)	40	26.0	4.1
Waist Circumference (cm)	40	85.3	7.8
Systolic BP (mmHg)	40	104.5	9.7
Diastolic BP (mmHg)	40	60.1	7.0
Resting Heart Rate	40	85.1	10.7
Glucose (mg/dL)	40	90.6	7.2
Hemoglobin A1c %	40	5.4	0.3
High Sensitivity CRP (mg/dL)	40	2.5	2.5
Fasting Insulin (mu/ml)	40	16.2	10.5
Fasting Cholesterol (mg/dL)	40	154.7	27.8
HDL-c (mg/dL)	40	44.2	11.6
LDL-c (mg/dL)	40	92.7	24.6
Triglycerides (mg/dL)	40	89.2	55.6
Non-HDL Cholesterol, Calc. (mg/dL)	40	110.5	29.0
24H Recall: Energy Intake/Day (Kcal)	40	1232.0	329.4
24H Recall: % Calories From Fat	40	29.5	4.8
# of Valid Accelerometer Week Days	40	5.2	1.0
# of Valid Accelerometer Weekend Days	40	2.0	0.2
# Of Valid Acceleromter Days	40	7.2	1.1
Children's Depression Index (10-40)	40	4.3	4.2

Baseline Child Measures	N	Mean	SD
Sleep Disordered Breathing (Hi:9 Lo:3)	40	3.7	0.9
Daytime Sleepiness (Hi:24 Lo:8)	40	14.0	2.7

		N	Percent
Tanner Male Pubic Hair:	Refused	1	7%
	Stage 1	4	27%
	Stage 2	8	53%
	Stage 3	2	13%
	Stage 4	.	
	Stage 5	.	
Tanner Male Genitals:	Refused	1	7%
	Stage 1	2	13%
	Stage 2	9	60%
	Stage 3	2	13%
	Stage 4	1	7%
	Stage 5	.	
Tanner Female Breast Development:	Refused	1	4%
	Stage 1	5	20%
	Stage 2	7	28%
	Stage 3	10	40%
	Stage 4	2	8%
	Stage 5	.	
Tanner Female Pubic Hair:	Refused	.	
	Stage 1	18	72%
	Stage 2	4	16%
	Stage 3	2	8%
	Stage 4	1	4%
	Stage 5	.	
Female Menarche:	No	25	100%
	Yes	.	
BMI Percentile:	85-94%ile	6	15%
	≥ 95%ile	34	85%
Country Born:	USA	38	95%
	Mexico	1	3%
	Other	1	3%
Covered by Health Insurance:	Yes	40	100%
Child Receives Reduced/Free School Food:	No	7	18%
	Yes	32	80%
	Don't Know	1	3%
Child care in home:	0 hours per wk	28	70%
	1-10 hours per wk	10	25%
	11-20 hours per wk	1	3%
	21-30 hours per wk	.	
	31-40 hours per wk	1	3%
	41+ hours per week	.	

		N	Percent
Child care in another home:	0 hours per week	37	93%
	1-10 hours per wk	2	5%
	11-20 hours per wk	1	3%
	21-30 hours per wk	.	
	31-40 hours per wk	.	
	41+ hours per wk	.	
Childcare Center:	0 hours per week	22	55%
	1-10 hours per wk	9	23%
	11-20 hours per wk	8	20%
	21-30 hours per wk	1	3%
	31-40 hours per wk	.	
	41+ hours per wk	.	
School Grades:	Don't Know	1	3%
	Mostly As	10	25%
	Mostly As and Bs	19	48%
	Mostly Bs	3	8%
	Mostly Bs and Cs	4	10%
	Mostly Cs	1	3%
	Mostly Cs and Ds	2	5%
	Mostly Ds	.	
	Mostly Ds and Fs	.	
	Mostly Fs	.	
# of working TVs:	1	6	15%
	2	21	53%
	3	10	25%
	4	1	3%
	5	2	5%
TV where child sleeps:	No	10	25%
	Yes	30	75%
Is there a computer in home?	No	10	25%
	Yes	30	75%
Desktop computer in child's bedroom?	No	34	85%
	Yes	6	15%
Laptop allowed in child's bedroom?	No	37	93%
	Yes	3	8%

Table 4.4. Select Index Parent Characteristics (Analysis Sample N=40)

Baseline Adult Measures	N	Mean	SD
Age (yrs)	40	38.1	7.3
Height (cm)	40	158.0	7.2
Weight (kg)	40	80.4	20.5
Body mass index (kg/m^2)	40	32.1	6.7
Waist circumference (cm)	40	106.5	14.9
Total years lived in US:	40	19.6	9.3
Medrich: Household TV Use (0-4)	40	1.9	1.1
# of adults living in household	40	2.9	1.7
# of children living in the household	40	2.9	1.7

		N	Percent
Country Born:	USA	7	18%
	Mexico	30	75%
	Other	3	8%
Marital Status:	Married	29	73%
	Divorced/Separated	6	15%
	Widowed	.	
	Single - Never Married	5	13%
Own home:	No	30	75%
	Yes	10	25%
How often speak English at home?	Never	9	23%
	Sometimes	19	48%
	About 1/2 the time	4	10%
	Most of the time	4	10%
	Always	4	10%
Employment Status	Declined to answer	1	3%
	Working full time	18	45%
	Working part time	9	23%
	Not working for pay	12	30%
Max Education Level Achieved:	6th grade (elementary school) or less	7	18%
	7th - 8th grade (attended some middle school/junior high)	4	10%
	9th - 12th grade (attended some high school)	9	23%
	High school graduate (received diploma or the equivalent, GED for example)	8	20%
	Completed some college credit, (or technical school) but no degree	6	15%
	Technical degree	4	10%
	Associate's degree	1	3%
	Bachelor's degree	1	3%
	Master's, Professional, or Doctoral degree	.	
Household Income:	Do not know	2	5%
	Prefer to not answer	2	5%
	14,999 OR LESS	8	20%
	$15,000-$24,999	13	33%
	$25,000-34,999	10	25%
	$35,000-$49,999	1	3%
	$50,000-$74,999	1	3%
	$75,000-$149,999	3	8%
	$150,000-$199.999	.	
	$200,000 or more	.	
Food Security:	High Food Security	24	60%
	Low Food Security	12	30%
	Very Low Food Security	4	10%
SNAP:	Refused	1	3%
	No	24	60%
	Yes	15	38%

		N	Percent
Government Aide:	Refused	1	3%
	No	34	85%
	Yes	5	13%
Exercise Weekly:	No	16	40%
	Yes	24	60%
# of days:	NA	16	40%
	1 day	1	3%
	2 days	5	13%
	3 days	7	18%
	4 days	.	
	5 days	6	15%
	6 days	4	10%
	7 days	1	3%
For how long:	NA	16	40%
	About 10 minutes	1	3%
	About 20 minutes	1	3%
	About 30 minutes	8	20%
	About 40 minutes	4	10%
	About 50 minutes	1	3%
	About 1 hour or longer	9	23%

Clinical Monitoring Results: With each data collection we screen participants for pre-existing or incident conditions that may pose a risk to their health, but are not expected to result from participation in the study. This represents an additional safety mechanism for study participants. Parents/guardians are notified and referred to their primary medical care provider for further evaluation and care as needed. Notifications and referrals are made in writing, with a full explanation, and followed-up with subsequent phone calls to answer questions and determine whether the child was medically evaluated. All reports (whether abnormal or not) are also faxed to their designated primary care source (see below). Of the 48 children assessed at baseline in the Pilot study we identified the following abnormal measures.

Table 4.5. Pilot baseline clinical monitoring results

	Classification	N	Percent
Height ≤ 5th %ile	≤ 5th percentile for age and sex	0	0
Systolic or Diastolic blood pressure	> 90th percentile for age, sex and height	8	16.7
	> 99th percentile plus 5 mmHg (stage 2)	0	0
Fasting glucose	> 100 mg/dL	4	8.3
	≥ 126 mg/dL	0	0
Fasting Total Cholesterol	> 170 mg/dL	8	16.7
	≥ 200 mg/dL	4	8.3
LDL-Cholesterol	≥ 110 mg/dL	8	16.7
	≥ 130 mg/dL	3	6.3
HDL-Cholesterol	< 35 mg/dL	6	12.5
Triglycerides	> 135 mg/dL	8	16.7

Post-test data collection and participant retention:

We delayed the start of post-test data collection by 3 weeks due to overlap with the Winter holidays. However, we are still achieving a high follow-up rate. To date, 22 families have completed their post-test data collection (with completion of all anthropometric/physical and survey measures) and only 2 of those pending are beyond the target measurement window.

Table 4.6. Pilot post test follow-up completion

Total N	N due for follow-up as of 3/9/12	Completed	Pending - on time (within window)	Pending - tardy (beyond window)
40	34	22	10*	2

* 5 of these 10 pending have already been scheduled for their data collection.

Completion rates for accelerometry and 24 hour diet recalls lag behind other measures, in that order, because they occur after the visits. To date, 14 of the 22 have completed at least 4 valid days of accelerometry and all three 24 hour diet recalls, another 3 have completed accelerometry, and 8 are still in the process of completing both accelerometry and their 2nd and/or 3rd 24 hour dietary recalls.

We are finding most of the measures are going well. One notable observation is that the parents/guardians in the Pilot study are having more difficulty completing self-administered questionnaires than we anticipated. All surveys are available in English and Spanish, but it appears we are attracting an even higher risk sample than in prior studies, including some parents/guardians who are unaccustomed to completing written surveys. As a result, we are now helping some parent/guardians complete their surveys as interviews. The issue appears to be not as much understanding the questions, but comfort with reading and answering written questions.

We also found that many parents reported not remembering information about their pregnancy, child's birth weight or length of breastfeeding. Therefore, we will not include those items in Phase 2.

Randomization and Interventions:

Our planned Phase 2 intervention spans 36 months. To start to test as many components of the intervention as possible during a 3 months Pilot study, we divided up the intervention into component parts. We randomized 10 families to receive health education control activities and 30 families to participate in one or more elements of the planned MMM intervention (all 30 after school sports, 15 screen time reduction, 15 behavioral counseling to improve diet). In addition, all 40 were included to send their baseline metabolic screening to their primary care providers.

Health Education (10 families). Families were sent 3 sets of newsletters on an accelerated schedule (for Phase 2 newsletters will be sent monthly). Child newsletters highlighted the topics of a welcome to the program, benefits of physical activity ("get pumped"), and eating breakfast. Parent newsletters highlighted the topics of inactivity, cholesterol, and eating breakfast. We chose these newsletters to have somewhat different types of topics and styles. As these 10 families complete the Pilot study we will obtain feedback on their response to the newsletters. We also held two, evening health education "Family Fun Nights" at community locations. All family members are invited to attend. One was focused on general health promotion and the other on basic nutrition. Attendance was as good or better than we would expect. Three of ten families (30%) attended the first and one of ten families (10%) attended the second. It is our experience that families request evening health education events but do not often attend. This has been the case in several of our past studies where we have included a health education control condition. However, because it is what they say they want and expect in terms of health education we still believe it is worth offering them and will continue to do so in Phase 2. The newsletters and health education events also represent the

current state-of-the-art of information-based health education to provide a rigorous control condition while meeting the expectations of the participants randomized to that condition (see discussion of control intervention in the Intervention section of the Protocol).

After-School Team Sports (30 families). We randomized 30 families to have access to the after-school team sports activities program. This was to be able to have a sufficient number to test activities at two different locations. Sessions are offered 5 days per week at the Menlo Park Clubhouse of the Boys and Girls Clubs of the Peninsula (BGCP) and Hoover Elementary School Redwood City Parks and Recreational Program (RWC). Our sports curriculum is based on our previous trials and we are enhancing it with the help of our Teams Sports Advisory Group. The Team Sports Advisory Group includes representatives from Boys and Girls Clubs of the Peninsula, Stanford Athletic Department, Team-Up for Youth/Coaching Corps, Positive Coaching Alliance, Bay Area Women's Sports Initiative, FitKids, Performance Science Training Institute, and PlayRugby USA, and meets quarterly and as needed to discuss best practices and continue to support partnerships among the various members.

The sports activities program runs from 3:30pm-5:00pm at BGCP and 4-5pm at RWC, to test two different scheduling approaches. A homework session is integrated into the existing programming at the community sites before and/or after our activities program. Our coaches also contribute as tutors during the homework session. Homework completion after sports is a challenge because of limited time. We have found the later start time is better for sports attendance and are working with our partners to schedule homework before our activities session.

The pilot curriculum is testing the four sports, (soccer, basketball, flag football and lacrosse) planned for Phase 2. Each sport was initially being introduced for a 3 week "season" (planned 3 month seasons in the Phase 2 trial). Based on feedback from coaches we expanded the seasons to 4 weeks of each sport to increase opportunities for mastery. We were unable to test 3 month seasons in the Pilot study but we believe they will be appropriate based on our experience in past studies. If they prove to be too long we have the option of adding additional sports. We are also arranging to have athletes from various Stanford Varsity sports introduce a variety of other sports during special integrated mini-seasons.

Daily 1 to 1.5 hour activity sessions include warm-up, skills and drills and scrimmages. A lead coach at each site is supported by 1-4 Stanford undergraduate interns at each practice. All coaches are trained on positive coaching techniques and promotion of growth mindsets in participants. We started by trying to include 4-5 different activities per session. We realized, however, that we could spend less time on group management and children would be more active if we included fewer different activities (3) per session and incorporated more variety into each activity. This also increased time spent in game-play which involves some of the highest intensity physical activity during the sessions. Another lesson learned was that breaking up participants into smaller groups favored more participation and one-on-one attention.

In addition, we are testing an innovation to emphasize the importance of hard work leading to improved performance. Feedback on skills improvement is motivating and consistent with the growth mindset framework. As a result, we are to providing objective feedback on skills acquisition. The skills challenge is being conducted during the first week of each sport. During the second week, a coach meets with a player one-on-one to set goals for the next skills challenge at the end of the sport. Performance is quantified and provided back to participants in real time. Below is an example of improvements in two of six Lacrosse skills assessed in the Pilot study.

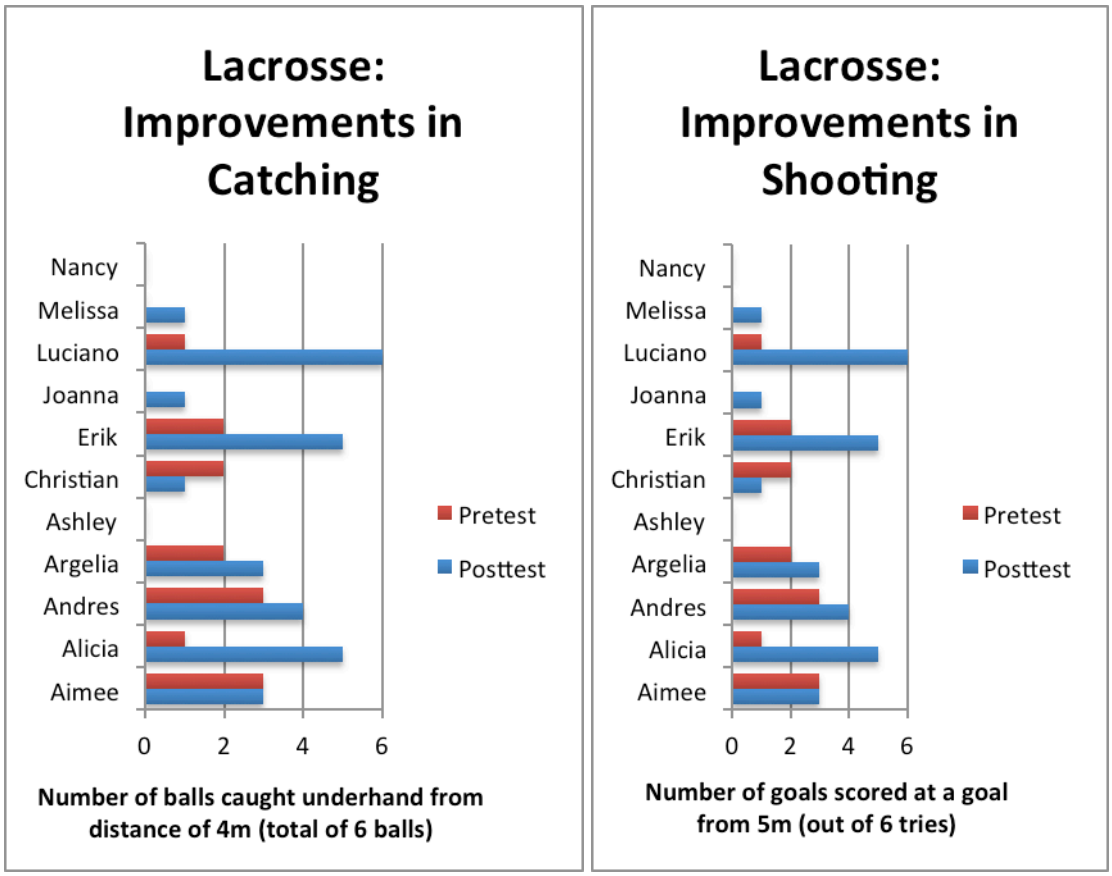


Figure 4.1. Sample skills challenge results

Participants have been highly responsive to this objective feedback. We have learned to offer it in a private, secure way, although the children do not seem particularly sensitive about sharing their results. Consistent with the growth mindset approach, children are encouraged to draw associations between the amount of effort they committed during “practices” and their changes in performance – emphasizing the relationship of effort to performance rather than fixed traits or pre-existing strengths and weaknesses.

To date, the sessions have been successful with many opportunities for learning to enhance the Phase 2 intervention. We found a need for additional staffing in the Pilot and two part-time coaches were hired as recruitment expanded to support a lead volunteer coach at each site. Coach to participant ratio has averaged 1:5 but ranges from 1:3 to 1:10 depending on the attendance and number of coaches available. The sessions run best with a 1:5 ratio or greater. However, we have not had insolvable problems with group control/discipline issues that could not be handled with even the lower coach to participant ratios. In Phase 2 we plan to have one employed lead coach at each site each day, supported by college student volunteers to achieve a desired coach to participant ratio of 1:5 or more.

One area of attention going into the Pilot study was the feasibility to handle the 7-11 age-span in the same sports sessions. We found that the activities we designed were engaging across the entire age range and proved feasible to implement. This may be helped by the population we are targeting. The majority of our overweight and obese children had not participated in sports to any significant extent in their recent pasts, somewhat leveling the playing field (so to speak). In addition, our emphasis on growth mindset encourages more individualized attention and a focus on effort to improving one’s own skills rather than constant comparisons with the rest of the group. We also

found that much broader age ranges were common in the after school programs and sports teams run at the same sites by our community partners. Therefore we did not find it necessary to break children into groups by age. However, we do break up into smaller groups to increase participation, intensity of effort and more one-on-one attention, demonstrating the feasibility of this approach for our current program. Therefore, if physical disparities start to manifest as problems over the longer time frame in Phase 2, we know we can perform drills and games in subgroups defined by size and skill level.

One additional challenge for an after school activities program is space. We work closely with our partner community sites and city recreation departments to insure adequate field space. BGCP has a gym that can be shared on foul weather days and several open spaces and parks within walking distance to the clubhouse. RWC has adequate adjacent field space but does not have access to a gym. On foul weather days we either use covered spaces or classrooms. One reason to include these two sites in the Pilot was to explore this variety of facilities availability. We have learned the multiple strategies to overcome these barriers and the bureaucratic, financial, and practical mechanics of acquiring access to indoor and outdoor space in different locations throughout the county. This will be invaluable for Phase 2. We also plan to try to limit our programs to sites with at least shared access to gyms or other appropriate indoor spaces.

Potential transportation barriers are addressed with each family once they were randomized to receive the after school program. In general, participants are either driven by family members, take a bus that provides transportation from schools, or are walked by our staff or community center staff as a "walking school bus." The Hoover school site is the easiest for access because it is on school grounds. However, this has also led to reconsideration of the timing of the sports program. Because children sometimes have difficulty arriving at the after school sites by 3:30, we are working with our after school program partners to schedule the Phase 2 sports activities program from 4-5 pm, to better insure participation for up to a full hour.

Attendance. Attendance rates have been excellent. Although many children are still participating in the pilot (range of possible days of attendance since randomization = 20 to 107). We currently are averaging an overall attendance rate of 61%. At the Menlo park BGCP site attendance has averaged 58% and among the smaller and more recent group at Hoover Elementary they are averaging 80%. For individuals, attendance rates range from 8% to 92%. These rates exceed our expectations compared to past after-school physical activity interventions and suggest that our program design and coaching is proving motivating to our target audience of overweight and obese children.

Performance feedback for coaches. Feedback has proven to be a particularly salient motivator to improve performance across many different learning and performance contexts. As a result, we are introducing a performance feedback system for coaches as part of our Pilot study. For this work we were fortunate to have the input of an expert in physical education research, Anthony D. Okely, Ed.D, Associate Professor of Education, and Director, Interdisciplinary Educational Research Institute, at the University of Wollongong, Wollongong, NSW, Australia, who spent his sabbatical with our team from July through December 2011. Tony helped us adapt the SOFIT direct observation system for use as a training and feedback tool for our coaches. We added a higher level of moderate-to-vigorous activity to the SOFIT activity intensity scale and coding for the amount of time spent in time management activities (aka instruction time, which we aimed to minimize in our sessions) and the amount of time spent in fitness, skills and game play activities (which we aimed to maximize in or sessions). Coaches are trained to code the three parameters using videotapes and then observe sessions either directly or on videotape. The figure below illustrates the data collected over approximately two months during the early period of our Pilot study. Coaches can use this feedback and their training to alter their performance and increase the amount and intensity of physical activity while minimizing instruction time. In addition to motivating coaches to improve their session management, we use this as a process measure to monitor intervention fidelity. We are also in the process of developing a measure of growth mindset-consistent coaching behaviors that can be added to our SOFIT-based direct observations.

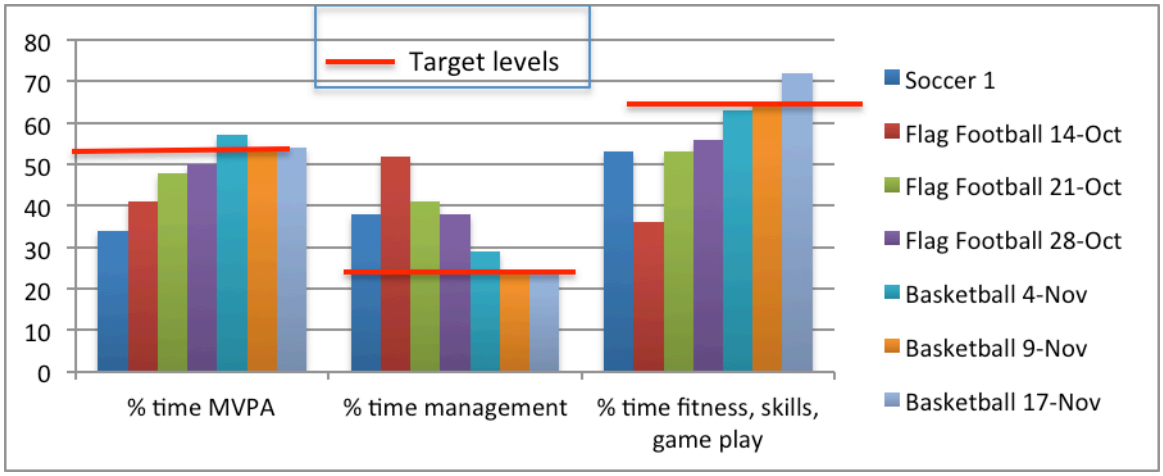


Figure 4.2. Sample SOFIT performance feedback

Physical activity intensity objective feedback trial. (Mary Rosenberger, an NHLBI-funded SPRC postdoc, with mentoring by Bill Haskell). As part of our after-school team sports pilot trial we also included testing of whether providing immediate (heart rate) and/or cumulative (pedometer steps) objective feedback would increase physical activity intensity among the overweight and obese children participating in our activity sessions. Based on the ubiquity of these gadgets, this type of objective feedback of physical activity is apparently useful and motivating for athletes in training and for exercisers at health clubs. However, we could not find much relevant published evidence for this apparent benefit in activity sessions, and no studies among overweight and obese children. If there is a benefit, we also want to learn the most feasible and effective way to introduce objective feedback into our activity sessions.

To explore this, on selected days individual children attending the after school activity session were randomly assigned to wear either a Polar Heart Rate Monitor with a wristwatch display, an Omron pedometer with number of steps displayed, or no objective feedback device. All children wore Actigraph GT3X+ accelerometers to assess activity intensity. Earlier pilot testing identified challenging but achievable goals for maintaining an elevated HR and for accumulating steps over the course of the entire session. Children were given those goals and asked to monitor their progress toward achieving them. Research assistants also recorded the times and types of activities being delivered during each segment of the session. Data collection just recently ended and the results are pending analysis. The results and implementation lessons learned will help us decide whether and how to include these types of direct feedback to participants as a regular part of Phase 2.

Home Intervention – Screen time reduction (15 families). We are conducting home counseling visits for screen time reduction with 15 families. For the Pilot study, each family is receiving a total of 5 visits. Currently families range in their progress, having completed from 1-5 visits, roughly related to their date of randomization. Four of the 15 families have completed all five visits to date. The visits focus on the main goals of creating temporary block out periods, developing a hobby as an alternative, and screen time budgeting. However, these lessons start with an introduction to "brainology" and a growth mindset, based on Carol Dweck's intervention studies to improve math performance in girls (see above). Children and their parents have been particularly enthusiastic about this framing in part, we believe, because it presents a fresh perspective compared to their expectation of being scolded for their behavioral lapses. The intervention then focuses on building skills and competence for two main screen time reduction strategies, reducing eating while watching screens and reducing total screen time.

We have found that children in our study are eating constantly and often in front of TV. To address this we ask that children establish eating routines and eat only at a designated spot at a table outside of viewing of a TV screen. We are also experimenting with using the TV time manager (BOB) to block out 2-hour periods during times that the child is most likely to eat while watching television. We also use the TV time manager to help children budget television viewing hours. We chose the BOB because of its ease of use. Our past studies used the TV Allowance which is more difficult to program and no longer available. Thirteen of 15 families have hooked up at least one BOB electronic TV time manager to a television in their home, with seven families hooking up two or more. This is about the number we would expect based on our past studies. We are finding some families are very excited to use the BOB while others are very resistant. Consistent with our past research, the main barrier has been a parent or grandparent who does not want their TV viewing interfered with, or a parent who claims they are unwilling to impose limits on another child in the household. However, we have also witnessed the use of TV as a babysitter and pacifier to reduce conflict within the household, and we believe this is more common than acknowledged. We have incorporated this experience and learning into our intervention approaches and will be continuing to test these in the ongoing Pilot study. We are also testing alternative strategies to help families monitor their viewing, reduce viewing while eating and budget their TV viewing hours without an electronic TV time manager.

Another barrier to BOB use has been technical. The BOB sometimes turns off or beeps spontaneously after prolonged use. This seems to be related to the low amount of power that is drawn by the newer, more energy efficient LED TVs. The BOB handles this better than the TV Allowance did, and we have identified several fixes that we can program into its firmware. However, if families are already skeptical about limiting their screen time then any hint of malfunctions and inconvenience can be a good excuse to reject the BOB. We are working with the manufacturer and our own engineers to develop additional solutions.

Home Intervention – Behavioral Counseling for Diet and Activity (15 families). In the Pilot study we are conducting only five home visits from our individualized Stanford Pediatric Weight Control Program. As a result, the visits try to cram in a number of skills (self-monitoring/journaling, traffic light food classification guidelines, counting red light foods, and creating a red light goal). However, like the screen time reduction lessons, we begin with basic “brainology” and an introduction to a growth mindset. This has also turned out to be an appropriate and motivating frame for changes in diet. To date, 10 of the 15 families have already completed 3 or 4 visits. We are finding families to be highly receptive to these lessons. Perhaps this should not surprise us because they are derived from our highly successful group program and have been improved accordingly, over more than a decade.

Primary Care Intervention (40 families). Due to the short, 3-month period of intervention for each family we focused our Pilot study efforts on establishing a practical and effective method to communicate results and updates with primary care providers. We did this with the reporting of metabolic and blood pressure baseline measures for all families. In Phase 2, this will also occur for all families at each measurement time point. Members of the MMM intervention group will also have more frequent intervention progress reports and SEFs reported to their primary care providers, so it is essential to identify a way to do so.

The first step was to collect information from participants on their primary source of medical care. It was unknown whether our high-risk, low-income participants would be willing and/or able to identify their source of primary care and their contact information. Out of the 40 families there was only one refusal. The remaining 39 families were willing and able to identify at least one primary care source by name. We attribute this high rate, in part, to our explanations of the value of sharing their metabolic and blood pressure measures with their primary care providers. However, it often required follow-up phone calls to get a provider or clinic name. Of these, 26 named a specific provider and 13

were only able to identify a clinic name (e.g., Kaiser, Lucile Packard Children's Hospital, Ravenswood family clinic). Together, these 39 families identified 24 different sources of primary care. Individual physicians and nurses were named only by 1-5 families and individual clinics were named by only 1-4 families, exhibiting a tremendous diversity. We also do not know how valid, reliable or stable these sources of care are. In Phase 2 we will need to review/confirm this information with each family at each data collection visit and more often with those randomized to the MMM intervention. This was a reality check for our intervention design. Learning that the diversity of sources of primary care was even greater than expected, squashed any impulses we had to try to intervene more directly with primary care providers to alter their broader practice approaches, and confirmed our plans to target their specific interactions with our participants.

A second challenge was collecting contact information for the identified sources of primary care. Our work with partner clinics suggested that fax was the most direct and practical way to communicate information to a patient's provider and/or chart. Most practices and clinics have adopted or are in the process of adopting electronic medical record systems but there is no consistency in the products they are using or the way they are customizing them. Therefore, we will not be able to transfer data directly into their medical records systems. Similarly, such a transfer would require patient identifiers of some type. Only 12 of 39 families were willing or able to give us a number they thought was their patient ID/Medical record number. In only a minority of cases did participants give us a primary care telephone number and in no cases did participants report a fax number. As a result, it became apparent that we needed to contact every primary care provider identified for their contact information. Although we obtain HIPAA authorization to share participant information with the primary care source they identify, their primary care sources do not have HIPAA authorization to share any information with us. Therefore, we are unable to confirm these sources of primary care or obtain patient identifiers from the primary care providers we contact. However, we were able to obtain fax numbers for all 24 different sources of care and successfully faxed baseline metabolic and blood pressure findings. Each report includes a summary of values as well as a copy of the letter that is sent to parents with the results and their interpretation. We also followed-up with a phone call to the primary care source 24-48 hours later to confirm receipt of the fax. Although we had electronic confirmations that all faxes were successfully received, a number of sources contacted directly could not confirm their receipt of the reports and asked us to repeat the fax, which we did. Our Pilot study results confirmed our formative research and our experiences in primary care, that have led to our primary care intervention design but it is clear that effective communication with primary care providers and clinics will continue to be a challenge for us in Phase 2.

4.2.4 Additional Phase 1 Formative Studies

Home Environment Dishware Intervention. We did not include a home eating environment intervention group in our Phase 1 Pilot study. This is because we are concurrently implementing a similar intervention as part of another large-scale clinical trial for obese children. Although the studies have different eligibility criteria and designs, we are still learning a tremendous amount that is informing our Stanford GOALS home environment intervention.

To date we have enrolled 6 cohorts of participants (3 English language and 3 Spanish language). Fifty-five of 111 families are randomized to the group that receives the home environmental strategies treatment intervention. There has been almost complete participation among treatment group families with home visits, including acceptance of smaller dishware (96%). We have been offering families six different styles of dishes and bowls to choose from (white, orange and blue, green, blue, black, and square white). The square plate has been most popular and the round plates with green and black rims are least popular, although all five have been selected. It appears we will need to continue to offer a variety of styles. We have supplied a Mean ± s.d. of 12.3 ± 3.6 plates, 12.4 ± 4.4 bowls, 11.8 ± 3.6 mugs and 14.4 ± 7.6 glasses per family. We

have learned it is sufficient to initially supply families with 2 place settings for each family member plus 2 extra settings. Families will then ask for additional place settings if needed. We have also found it is easier to leave existing dishware that complies with our size limits than to remove it from the home. Dishware and glasses that are larger than the size criteria are packed away. We have removed an average of 17.9 plates, 13.9 bowls, 8.9 mugs and 13.1 glasses from participating households. This includes most dinner plates, glasses, coffee mugs and bowls, all rimless plates unless diameter is smaller than 7 inches (the size of a saucer), all soup bowls (plates), regardless of volume or diameter. All families appear to have accepted the dishes and are using them consistently. One important finding is that families have been willing to use the smaller dishware throughout holiday seasons (Thanksgiving, Christmas, Passover).

Some parents have been particularly reluctant to part with the large coffee mugs they use daily. In these cases parents may be left with one coffee mug each, but only if they insist. We are providing new mugs. Other things we have learned not to take: Anything of sentimental or monetary value that they do not want us to take may be packed and stored in their home -- we can provide a box and packing materials; China only used for special occasions; Bread and butter plates, very small bowls and small glasses may be left if they are smaller than our threshold measures; Water bottles and thermos bottles. The vast majority of families agree to let us take their dishware and store it in a storage unit. Families with more expensive dishware often request to store their own dishware in their basement or garage. We securely box all the dishes in these instances and help the family put them into storage.

During the design of the program we anticipated difficulties in implementing the home-based intervention for families where the child lives in multiple households. For these families we try to gain full participation of all households but we also use a modified intervention to implement in secondary households when the child's time is primarily spent in one household (consumes four or fewer meals per week in a second, third or more households, including parent, grandparents or other caregivers). This has proven to be a successful strategy for this situation and has made it possible for more families to participate.

Visual Illusion plate study. As part of Phase 1, Stanford GOALS Early Stage Investigator (ESI) and NHLBI-funded postdoc Arianna McClain has been conducting an additional pilot study on plate design, to complement the formative research on replacing dishware. Dr. Sam McClure, our other Stanford GOALS ESI, is also collaborating with Dr. McClain on this study. Prior research finds direct relationships between perceived food portion size (FPS) and intake. The Delboeuf Illusion affects perceptions of the relative sizes of concentric shapes. This study applied the Delboeuf illusion to food on a plate, testing the effects of varying rim widths and designs on perceived FPS. The ultimate goal of this work is to identify the optimal plate design for use in Phase 2.

The study used a within-subjects experimental design. Participants were recruited via Amazon's Mechanical Turk and observed photographic images of paired, side-by-side plates containing the same or different amounts of food. From each pair, participants were asked to select the plate that contained more food. In Study 1, 338 participants completed 42 trials each (7 FPS X 6 rim widths; no rim and 1/8, 2/8, 1/3, 3/8, and 4/8 rim width to plate radius ratios). In Study 2, 251 participants completed 28 trials each (7 FPS X 4 rim designs; no design, solid blue rim, line around inner edge of rim, lines around inner and outer edge of rim). A multivariable logistic regression examined the effects of depicted FPS and rim characteristics on perceived FPS.

The results indicated that participants overestimated FPS on plates with wider rims and rim designs. Study 1: rim width ($P<0.0001$) and depicted FPS ($P<0.0001$) had significant effects on the odds of perceiving larger FPS, and an optimal rim width to plate radius ratio was identified. Study 2: confirmed findings from Study 1 and found a significant rim design X depicted FPS interaction ($P=0.0002$). On plates with rim designs, perceived FPS overestimation increased when depicted FPS decreased.

These finding suggest that the Delboeuf illusion applies to food on a plate. Manipulating plate rim sizes and designs affect perception of FPS. Wider rims and rim designs create visual illusions that exaggerate the perceived amount of food on the plate, and the effects of rim designs are greater with smaller FPS. We are now using these findings to identify the optimal plates to use in Phase 2. Dr. McClain is continuing this line of research and has been submitting applications to fund studies in children and on self-service and intake as they relates to plate design.

Measurement Development. We are also using the Phase 1 Pilot study to develop and or refine some of our measurements. All measures were tested but a few efforts deserve to be highlighted.

Implicit theories/Growth Mindset: during Phase 1 we have been developing a measure of implicit theories of weight, habits (in general), sports ability, and eating habits, based on the work of Carol Dweck.[106, 107] We started with the measures she has used in studies of mathematics and adapted them to the relevant topics. For our younger and lower literacy, predominantly Latino children and parents, we also simplified the response scales. In baseline testing we found that the items were understood and the simplified response scales still produced satisfactory variability in responses. We also learned that we can probably eliminate the reverse phrased items to reduce potential confusion without limiting variability. We are working with Professor Dweck on finalizing these measures in time for use in Phase 2.

Waist circumference. In past studies we have used the umbilicus as the landmark for measuring waist circumference in preadolescent children. In the present study the suggestion was to use the iliac crest. Finding this landmark requires more touching and poking which can be uncomfortable for young children. Therefore, we are conducting feasibility testing and comparing the results of measures in the two spots in obese children. Our impression is that the iliac crest measures are feasible and we plan to use this method in Phase 2.

Blood Pressure. In past studies we have measured blood pressure and resting pulse with the Dinamap Pro 100 automated monitor. In an effort to standardize methods with the study at Case Western Reserve (the only other field site measuring blood pressure), we have switched to the Omron HEM-705-CP, which is substantially less costly. However, we have had difficulty using this Omron model with our 7-11 year old overweight and obese children. When following the detailed MOP and Omron instructions, it frequently produces erratic, extremely high results or error messages in a large number of children. When this occurs we remove the cuff and restart the procedure from the beginning. However, this does not always correct the problem, even when we switch data collectors or, in some cases, retry on another day. However, for purposes of clinical monitoring we always repeat the measures with the Dinamap Pro 100 which has always produced reliable results. We continue to attempt to sleuth out the causes, adjusting techniques and data collectors to try to identify a systematic problem, and have consulted with the manufacturer and other investigators who have used Omron devices in population studies. Our current hypothesis is that it is a cuff problem. The Omron HEM-705-CP has 3 possible cuff sizes for adults, small, medium and large, but no pediatric-sized cuffs. The choice of the proper cuff size is based on the arm circumference. Our overweight and obese children tend to have upper arms with substantial circumferences (generally in the Omron adult medium cuff range) but are likely to have upper arm lengths that are short relative to their circumferences. It is possible that the Omron cuffs have difficulty if their width is too great for the length of the upper arm. We are now experimenting with different positions of the cuff and the tubes exiting the cuff, although still consistent with their directions. This needs to be resolved prior to Phase 2. This is not only a problem for obtaining accurate measures of blood pressure but the erratically high values also have been classifying children as having stage 2 hypertension requiring immediate medical care evaluation and often a trip to the emergency department, according to our protocols and good clinical practice. Fortunately, we have been able to assure ourselves that these elevated readings are all false positives when we recheck with the Dinamap. However, this back up approach is not feasible for Phase 2.

Analysis Approaches*.* As part of Phase I, we explored a number of analysis issues in planning for Phase 2. Among other smaller studies, the main issues were assumptions about the shape of the expected BMI trajectory in our study and whether robust standard error estimates were protective in designs in which cluster membership is mistakenly assumed to be present when it is not, or when it is misspecified when it is present.

Linear BMI trajectory assumption: To help determine whether a linearity assumption is appropriate for BMI changes for the Stanford COPTR trial we examined BMI data from four prior longitudinal studies or RCTs performed at Stanford (see figures below). We limited these analyses to the participants in these studies that would most closely represent our proposed study sample in terms of age, baseline BMI ≥ 85th percentile for age, and ethnicity. Our investigation involved three different approaches.

Evaluation of graphical trends of observed BMI over time for each treatment arm (for those studies with multiple treatment arms), for each age group at entry, and for gender. Graphical evidence for linearity is strong. The figures below present the average observed BMI at a given time point for each group over time and largely demonstrate a linear trend over the study periods. These results are consistent with the published trajectories of BMI illustrated in the literature identified by the RCU.

Assessment of coefficients from more flexible, mixed effects regression models that allow BMI change to be non-linear over time. The coefficients correspond well to the plots and demonstrate monotonic increases in BMI over time and, in general, largely linear trends.

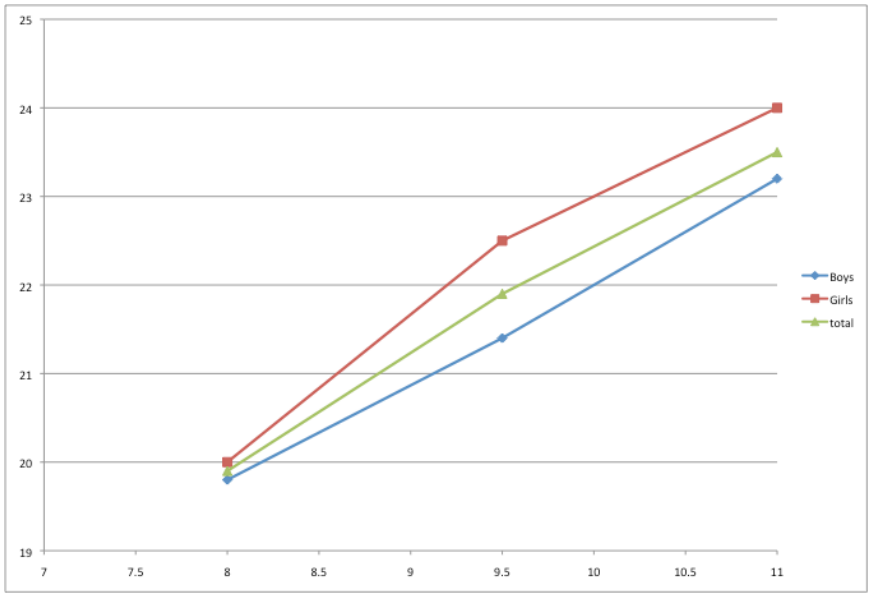
A formal test comparing a model assuming linear changes in BMI over time versus one that assumes a quadratic relationship between BMI and time (including both a linear and squared term). The test of the null hypothesis was performed for each relevant subgroup (18 tests across the four studies) and the null hypothesis was rejected in one case (ECHALE study, age 8, control group).

Summary: The findings from all three approaches support the assumption that BMI changes are linear over the Stanford COPTR age range. Our findings are also consistent with the trajectories shown in the published literature and is expected when fitting four annual timepoints. Based on these results, we believe an assumption of linear changes in BMI over the study period, with annual measures for both treatment and control arms, is reasonable.

Growth Study

Agras WS, Hammer LD, McNicholas F, Kraemer HC. Risk factors for childhood overweight: a prospective study from birth to 9.5 years J Pediatr. 2004 Jul;145(1):20-5.
Agras WS, Bryson S, Hammer LD, Kraemer HC. Childhood risk factors for thin body preoccupation and social pressure to be thin. J Am Acad Child Adolesc Psychiatry. 2007 Feb;46(2):171-8.

Type: Observational, recruited from well nursery at 3 local hospitals
Gender: Boys and girls
Ethnicity: Mostly Caucasian
Measurements: ages 8, 9.5 and 11
Wt. sample ≥ 85%ile

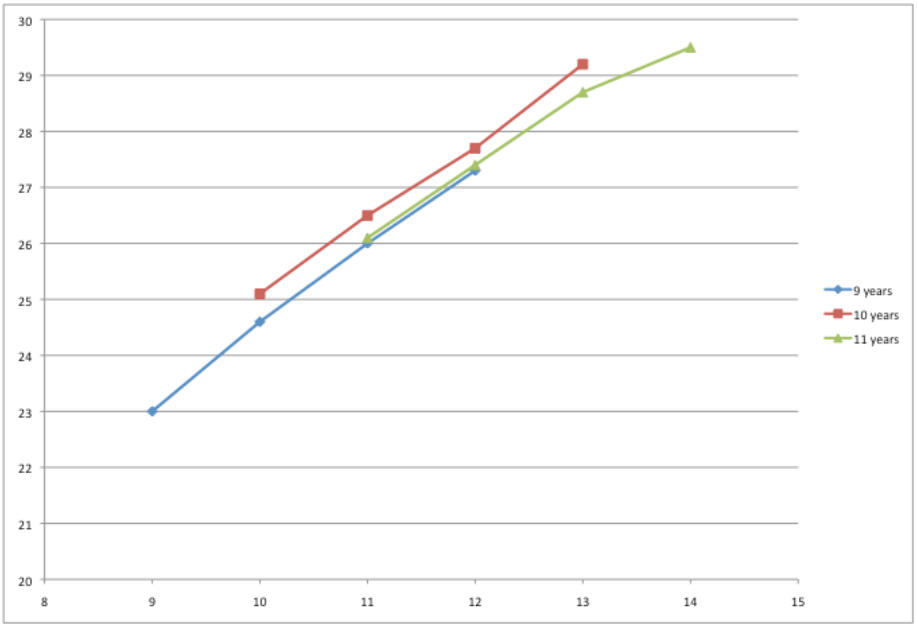


		Approach 2		Approach 3	
	Sample Size	beta□coefficient 1.5yr	beta□coefficient 3yr	Log likelihood ratio	P value
Boys	12	1.6	3.4	.062	0.89
Girls	9	2.5	4.0	1.178	0.42
Total	21	2.0	3.6	.405	0.67

McKnight Risk Factor Study

The McKnight Investigators. Risk factors for the onset of eating disorders in adolescent girls: results of the McKnight Longitudinal Risk Factor Study. Am J Psychiatry. 2003;160:248-254.

Type: Observational , recruited from schools in 2 cities
Gender: Girls
Ethnicity: Mixed, relatively high proportion Hispanic
Measurements: yearly for 4 years
Wt. sample ≥ 85%ile

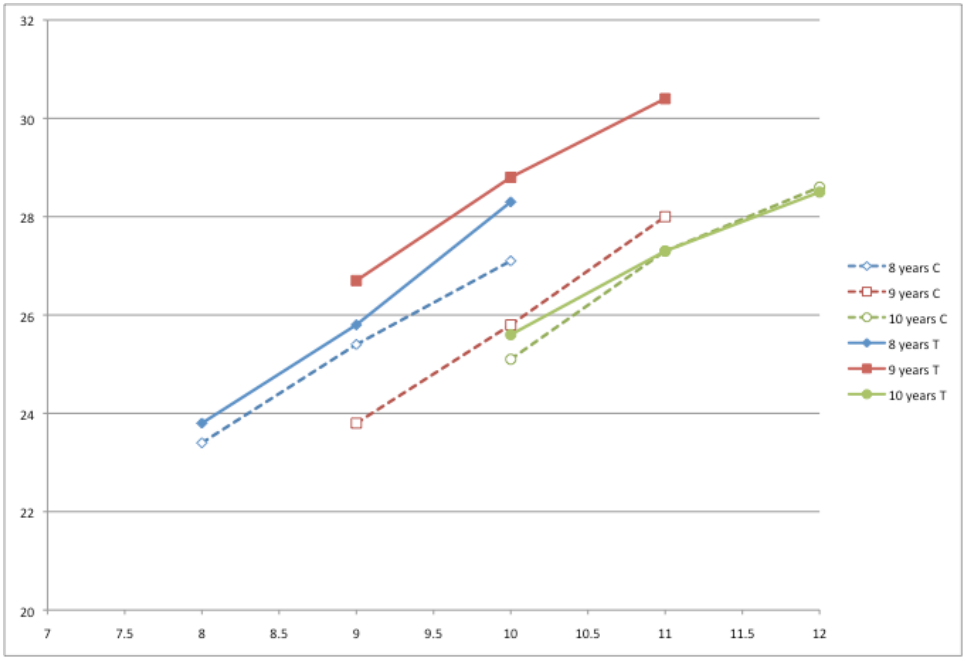


		Approach 2			Approach 3	
	Sample Size	beta coefficient 1yr	beta coefficient 2yr	beta coefficient 3y	Log Likelihood ratio	P value
age 9	64	1.57	3.02	4.25	.908	0.49
age 10	65	1.35	2.57	4.03	0.075	0.87
age 11	55	1.27	2.55	3.36	1.247	0.40

Stanford GEMS

Robinson TN, Matheson DM, Kraemer HC, Wilson DM, Obarzanek E, Thompson NS, Alhassan S, Spencer TR, Haydel KF, Fujimoto M, Varady A, Killen JD. A randomized controlled trial of culturally tailored dance and reducing screen time to prevent weight gain in low-income African American girls: Stanford GEMS. Arch Pediatr Adolesc Med. 2010 Nov;164(11):995-1004.
Type: RCT, recruited from low income areas in Oakland, CA

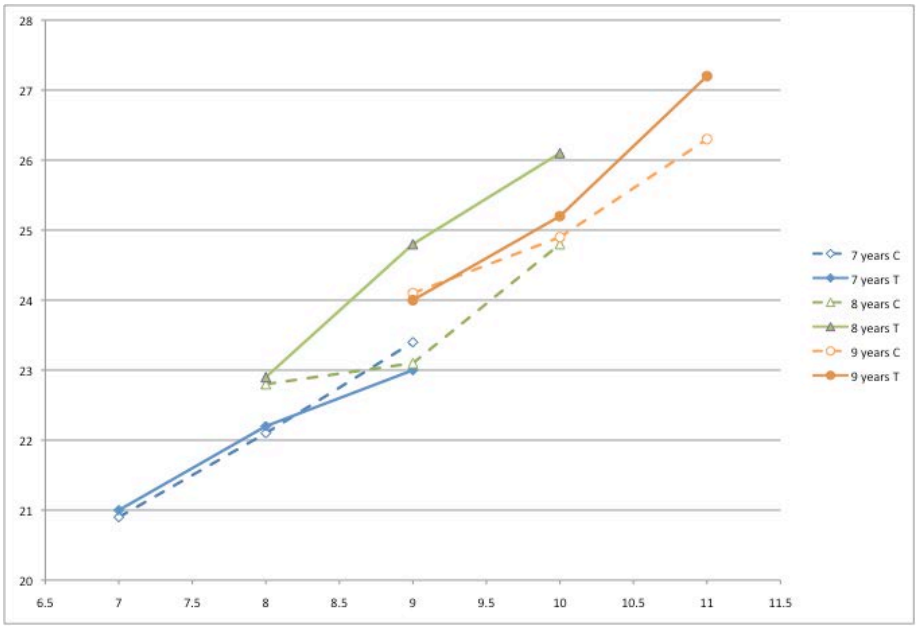
Gender: Girls
Ethnicity: African-American
Measurements: Yearly
Wt. sample ≥ 85%



			Approach 2		Approach 3	
		Sample Size	beta coefficient 1yr	beta coefficient 2yr	Log likelihood ratio	P value
control	age 8	15	2	3.7	0.097	0.85
	age 9	21	2	4.2	0.059	0.89
	age10	12	2.2	3.5	1.273	0.39
treatment	age 8	13	2	4.5	0.219	0.77
	age 9	13	2.1	3.7	0.331	0.71
	age10	13	1.7	3	0.244	0.75

ECHALE

(Manuscripts in progress)
Type: RCT, recruited from low income areas
Gender: Girls
Ethnicity: Latina
Measurements: Yearly
Wt. sample ≥ 85%



			Approach 2		Approach 3	
		Sample Size	beta coefficient 1yr	beta coefficient 2yr	Log likelihood ratio	P value
control	age 7	33	1.2	2.5	0.024	0.93
	age 8	16	0.3	2.0	6.107	0.03
	age 9	13	0.8	2.3	0.733	0.54
treatment	age 7	26	1.2	2.0	1.263	0.40
	age 8	24	0.9	2.2	0.511	0.62
	age 9	13	1.2	3.2	0.62	0.58

Robust standard errors simulation study

Knowledge of our study design suggests a very low likelihood of inducing clustered responses of participants and, if clustering were to exist, it would be expected to be very small, difficult to accurately define, and variable over time (see Analysis section for a detailed rationale of this conclusion). However, ignoring clustering when it is present risks underestimating standard errors and inflating type I error rates. One suggestion from an RCU investigator was to use robust standard error estimates (also known as sandwich estimators) as protection from inflated type I error if our assumption of independent observations is incorrect. An existing literature is not available to guide us regarding this question, and we were concerned that applying robust standard errors, which have their own set of strict conditions, would pose a risk if wrongly assuming clustering and/or clusters are misspecified. Therefore, we undertook a simulation study to evaluate the use of robust estimators of standard errors when clustering of subjects may be induced by the study design but cluster membership is unclear.

Study Design: We conducted simulation studies for a two-arm study, where the number of clusters varies (0, 4, 20 and 50), where the intracluster correlation varies (ICC=0, 0.001, 0.01, 0.09, and 0.50), where the sample size varies (N=100, 200, and 1000), and in the presence and absence of a treatment effect (beta = 0 and beta = 0.5). Unclustered data were generated from a linear regression model with normally distributed errors, and clustered data were generated from a mixed effects model with normally distributed errors and cluster-specific random intercepts. For each data set, in addition to the true model from which the data were generated, an OLS model was fitted and robust standard errors were estimated under each of 25 clustering assumptions that misspecified the true membership. Additionally, if the data were generated from clusters, an OLS model was fitted with robust standard errors estimated under the true cluster structure as well as under 6 clustering schemes that partially misspecified membership.

Results: Biased estimates of the variance resulted from misspecification of the true cluster membership, consequently inflating the type I error rate. Robust standard errors that assumed clustering of independent data yielded type I error rates of up to 40%. Robust estimators assuming partial and complete misspecification of membership (where some and no knowledge of true membership was incorporated into assumptions) for data generated from a large number of clusters (50) with a very high ICC (0.50) yielded type I error rates that ranged from 8%-12% and 18%-52%, respectively; assuming independence gave a type I error rate of 17%. When the ICC was weak ($\leq$0.01), nominal type I levels were achieved when clustering was ignored, whereas robust estimators that even partially misspecified membership resulted in an inflated type I error.

Conclusions: Robust estimators of standard errors can be useful when the ICC and the knowledge of cluster membership are high. When the ICC is weak, assuming independence has little consequence on the variance estimate, whereas misspecifying membership carries a high risk of inflated type I errors. Our study demonstrates that misspecification of the clustering membership matters, even when the data arise from a sufficiently large number of clusters. The implications of this are a high probability of falsely rejecting the null hypothesis. Therefore, while robust standard errors may be used to provide protection against misspecifying the correlation structure of clustering, they do not protect against misspecifying cluster membership.

Our study points to the need to make careful and thoughtful assumptions about both the correlation and clustering structure in choosing an analysis strategy for potentially clustered data. If the errors corresponding to subjects' outcomes are uncorrelated, results can be misleading by incorrectly assuming correlation exists. Similarly, even if subjects are clustered and the number of clusters is sufficiently large, results can be misleading if clustering membership is misspecified. In these cases, an OLS model that assumes independence is superior to one that completely misspecifies the structure.

In many cases, one is likely to have some information on cluster membership. Partial misspecification was found to produce lower type I error rates than assuming independence in some cases if the ICC is strong. This partial information about cluster membership, although imperfect, may improve performance. When the data are weakly clustered in an unclear manner, however, assuming independence produces comparable type I error rates to partial misspecification, provided the design effect is not large. Furthermore, the implications of misspecifying cluster membership can be high. When the ICC is weak and confidence in membership is not high, we recommend assuming independence. In addition, if data are generated from a small number of groups, robust estimation of the standard errors even under correct specification is not recommended. In this case, it is even more important that one try to determine the true conditions from which the data were generated.

David Murray and colleagues at Ohio State University also ran simulations of a slightly different nature. However, they too concluded that robust standard error estimates should not be used. Both Stanford and OSU are in the process of submitting their simulation studies for publication. Additional simulation studies are continuing.

These simulation studies have helped increase our confidence that our analysis plan is most suitable for our study design.

4.3. Key Recommendations for Phase 2

Many important lessons learned from Phase 1, and key recommendations for Phase 2 are described in the section above and in the descriptions of the methods below. However, here we highlight a smaller list of the key changes in our study design and protocols that have resulted from our Phase 1 formative studies, to date.

Recruitment, enrollment/randomization
• The recruitment and enrollment/randomization period has been extended to 18 months.

MMM Intervention
• We are adopting a unifying implicit theory/growth mindset frame throughout our home and after-school sports intervention components.
• We have added components of behavioral counseling for reducing dietary energy intake and increasing physical activity to the home/family intervention, based on the successful Stanford Pediatric Weight Control Program.
• We are introducing participant “choice” into the order of delivery of the home visit components to provide a more tailored intervention according to the perceived needs of the families without losing consistency in intervention content. The home intervention will start with home environmental changes (e.g., dishware) followed by the four 6-9 month modules (screen time reduction, diet changes, increasing physical activity, and problem solving) in order of participant preference.
• We will start with 3 after-school activity sites but plan to expand quickly to a total of 4-6 sites within the first year.
• We are enhancing our use of objective feedback to participants and coaches to motivate performance in the after school team sports intervention.

Enhanced Standard Care/Health Education Control Intervention
• Addition of home/family visits to increase apparent similarities between treatment arms and produce greater study engagement and contact for promoting greater participant motivation and retention for follow-up measures.

• Addition of field trips to promote greater study engagement and contact.
• Paid membership for a community center after school program will no longer be included, to reduce the appearance and confusion of two related but exclusive programs in the same sites.

Measurement
• Use of a COPTR common laboratory for metabolic measures

There may be additional changes and enhancements once we have the benefit of the completed pilot study.

5. STUDY POPULATION AND ELIGIBILITY

5.1. Eligibility Criteria

On the date of randomization, children must be:

- 7-11 years of age;
- BMI ≥ 85th percentile for age and sex on the 2000 CDC BMI reference.

5.2. Exclusions

To enhance internal validity, children are not eligible if they…

• Have been diagnosed with a *medical condition affecting growth* (a genetic or metabolic disease/syndrome associated with obesity, Type 1 diabetes, Type 2 diabetes taking medication, chronic gastrointestinal diseases, Chronic renal diseases, uncorrected structural heart disease, heart failure, heart transplant, anorexia nervosa or bulimia nervosa or binge eating disorder (present or past), AIDS or HIV infection, pregnancy);

• Take *medications affecting growth* (systemic corticosteroids more than 2 weeks in the past year, insulin, oral hypoglycemics, thyroid hormone, growth hormone);

• Have a *condition limiting their participation in the interventions* (e.g., unable to participate in routine physical education classes at school, requiring oxygen supplementation for exertion, developmental or physical disability preventing participation in interventions, children or parents/guardians who cannot medically participate in mild dietary restrictions and/or increased physical activity for any reason);

• Have a *condition limiting participation in the assessments* (child or primary caregiver not able to read surveys in English or Spanish, child two or more grade levels delayed in school for reading and writing in her native language);

• Are *unable to read, understand or complete informed consent in English or Spanish*;

• *Plan to move from the San Francisco Bay Area within the next 36 months*.

• Are deemed to have another characteristic that makes them *unsuitable for participation in the study* in the judgment of the Principal Investigator.

5.3. Inclusion Statement

(a concise definition that operationalizes who is in the permanent study denominator)

The study will follow intention-to-treat principles. All participants who are randomized will be enrolled in the study, regardless of their subsequent participation in study-related activities.

6. RECRUITMENT AND RETENTION

6.1. Recruitment Tracking

240 7-11 year old overweight and obese participants will be recruited over 18-months through primary care providers and clinics, schools, community centers and other community locations in East Palo Alto, Menlo Park, and Redwood City, CA. Primary care providers, clinics, schools, community centers, and others in the community will be informed of the study and criteria for eligibility. We will provide IRB-approved study recruitment materials and hold recruiting events throughout the community. Interested prospective participants will be asked to contact the research team directly. Once contacted, our study personnel will explain the study, answer all questions, and complete a brief, IRB-approved screening questionnaire to determine preliminary eligibility. Parents not sure about their child's height and weight will be offered the opportunity to be measured. Participants identified by screening to be potentially eligible will be invited/scheduled for a visit to sign informed consent, assent and HIPAA authorization to be formally screened and assessed for eligibility for study enrollment.

We will track participants from their initial contact through screening, consent, baseline measures, and randomization along with reasons for not continuing if they are lost along the way. We will use our own study-specific list of reasons for ineligibility and not-continuing that will then be categorized and reported monthly to the RCU using the methods specified by the Recruitment, Consent, Retention, and Adverse Events (RCRAE) subcommittee. These include the number screened, the number eligible (after screening), the number completing consent (which includes assent and HIPAA at Stanford), and the number randomized. Reasons are provided for not continuing at each step.

6.2. Recruitment of Minorities

We will recruit specifically from neighborhoods in East Palo Alto, Menlo Park and Redwood City with high rates of low-income, ethic/racial minorities. Based on the racial/ethnic composition of these communities and our experience in prior studies, we estimate the participants will be 50% female, and atleast 58% Latino/Hispanic, 15% Black/African-American, 12% white, 10% Pacific Islander, 3% Asian, and 2% Native American/Alaska Native. In our Pilot study in just two neighborhoods, our sample was 94% Latino/Hispanic, 4% Black/African-American and 2% multi-racial.

6.3. Procedures for Obtaining Informed Consent

Prior to baseline data collection, participation will be explained to children and parents/guardians in their preferred language (English or Spanish) along with potential risks and benefits and their rights to withdraw their consent at any time without prejudice. Signed consent will be required from parents/guardians (for themselves *and* for their child), signed assent will be required from the children, and signed HIPAA authorization will be required from parents/guardians prior to participation. All recruitment and consent procedures will be approved by the Stanford University Administrative Panel on Human Subjects in Medical Research (IRB).

6.4. Randomization Procedures

Children and their families will be recruited over an 18-month period. All interested children within a family will be assessed for inclusion in the study. One child will be randomly selected per

family for randomization and inclusion in analysis for families that contribute multiple eligible children. While one child per family will be randomized to a treatment condition, the treatment condition will be applied to all study eligible children belonging to that family (i.e., all participating children in a single household will be randomized to the same condition, and will be included in all intervention activities and measures). We include only one child per family to avoid violating the assumption of independent observations and inflating Type I error, while maintaining the integrity of the analysis. We do this blindly at the time of randomization, so as not to bias interventionists or data collectors to treat the analysis child differently than other children in the same household. Only the statistician is aware of which child in a multi-child household is in the analysis sample. By randomly choosing the analysis child from each household, regardless of their level of subsequent participation, we also avoid introducing bias (and maintain the intent-to-treat analysis). This is an important design feature because a number of families will have multiple participating children or live in multiple-family households.

Children will be randomized to treatment and control conditions *after* completion of *all* baseline measures. This includes completion of height, weight and all other anthropometric measures, all 3 24-hour dietary recall interviews, accelerometry for at least 4 days (3 weekdays and 1 weekend day) of at least 6 hours of at least 33% non-zero epochs per hour, all survey instruments attempted or completed, and fasting blood samples attempted or obtained.

Randomization Tool and Implementation: Efron's biased coin randomization,[89] where the allocation probabilities for any assignment are altered according to the number of participants already assigned to the different arms will be employed. To promote a balanced randomization on key characteristics that may influence weight changes, randomization will be done by applying Efron's technique within strata defined by BMI percentile at baseline (≥ 85th and < 95th percentile, ≥ 95th percentile). As it is important to include all stratification variables in the model, baseline BMI will be included in the primary model of interest.

Randomization will be performed by the statistician in SAS. Randomization will be performed at least once per week for families that have completed all baseline assessment. Order of randomization assignment will be done according to date of assessment completion.

A FileMaker database will be used to assure that those selected for randomization have met all eligibility requirements (from screener, baseline measures completion, baseline BMI eligibility, baseline age eligibility and consent completion). Only records that show as complete in FM will be randomized. Siblings will only be randomized once all have completed eligibility requirements.

Once subjects are randomized, they are in a separate randomization database with treatment assignment, randomization date, and analysis child assignment.

Security and Blinding: With our randomization technique, we are unable to anticipate subsequent randomizations. In addition, the database, which is stored on the FileMaker server, is secured.

• Only the data team can enter the randomization database values (with checks to prevent inadvertent overwriting), and modification will be prevented after assignment. More specifically, the randomization database, linked within FileMaker to other tables has its own permission settings.

• Interventionists have access to see treatment assignment (but not which sibling within a family is identified as the index child). Individual participants' assignments are viewable by all intervention staff on a participant level in order to easily deliver and track intervention delivery. Interventionists have access to contact information and intervention information, but will not have access to baseline data (once randomized) or any follow up data from data collection.

• Data Collectors can see randomization date, but not treatment assignment or index child assignment. Data Collectors will have access to contact information and data assessments (but limited once completed), as well as randomization date (used to generate targeted follow up dates.

• The investigators and all assessment staff will remain blinded to experimental assignment until after the final follow-up assessments are completed.

6.5. Techniques for Retention

Internal validity is threatened by differential attrition. We include many strategies to enhance trust and identification with our study as a whole, as described in the intervention and measurement sections, but we also include a number of strategies specifically designed to limit attrition.

• Enrollment is not be complete, and subjects are not randomized until *after* they have complied with all eligibility requirements and completed all baseline assessments. After initial recruitment into the study, families have no more than one month to complete all eligibility criteria and baseline assessments. This acts as a mild run-in process, selecting for those families potentially most likely to be able to complete the study.

• Each family is compensated for their participation in the study. Each family receives a total of $250 for participating in all scheduled assessments: $50 for completing the baseline, 12- and 24-month assessments, and $100 for completing the final 36-month assessment. Although most families tell us that financial compensation is not necessary, and not an important reason for joining the study, our experience is that compensation for time and participation helps some families to complete measures.

• If families are unable to complete the 12-, 24- or 36-month follow-up measures in the clinic, we obtain them in their homes. This method reduces attrition, improves the timeliness of assessments, and helps make the study sample much more generalizable and representative of our low-income target population.

• To be able to continue to find families who move without warning, we collect contact information for each family (a minimum of three non-household members who will always know where to find them). For families that move within the greater San Francisco Bay Area, data collectors travel to their new homes to collect measures. For families that move >100 miles, we will arrange for height and weight to be obtained by a local health professional following standard protocols, and families will be interviewed by phone. Prior to analysis, these data will be compared to all other data for evidence of measurement bias.

• Formative research is being conducted to identify the most appropriate non-monetary incentives to produce long-term participation in the study (study t-shirts, backpacks, lunch sacs, and caps have been favorites in the past).

• We utilize an active-placebo control intervention as our comparison condition to minimize differential attrition and provide the best test of our experimental intervention (described in more detail below).

In addition, a Retention Working Group is reviewing the extant literature on recruiting and and retaining low-income and ethnic/racial minority participants in research, and the Recruitment, Consent, Retention and Adverse Events (RCRAE) and Intervention subcommittees are reviewing and sharing the details of their experiences among the four field sites to enhance retention strategies in all studies.

7. INTERVENTION

7.1. Conceptual Framework

Bandura's social cognitive model serves as the foundation upon which all our interventions are based. In social cognitive theory, behavior develops, is altered and maintained through the interplay of personal, behavioral and environmental factors (termed "triadic reciprocality.")[115, 116] With respect to our intervention focus, personal (cognitive) factors include a child's and parent/guardian's own value systems which determine the nature of the incentives which influence eating and activity patterns, expectations derived from observation and experience about the consequences of different behaviors (outcome expectancies) and expectations about personal abilities to perform behaviors which will secure desired outcomes (efficacy expectancies). Behavioral factors include the skills available in the behavioral repertoire of the child or parent, and the degree of competence attained in using these skills. Environmental factors include peers, other family members, teachers and even media figures who model various attitudes and behaviors regarding eating, physical activity, parenting behaviors, etc., and are in a position, through their own actions, judgments or social positions, to influence the development of the participant's value system and standards of conduct regarding those attitudes and behaviors. Environmental factors also include environmental or structural influences such as televisions in kitchens and bedrooms, safe playgrounds and the availability of after-school and weekend activities, as well as the environmental influences on eating that we are manipulating in this trial, glass, plate, bowl and serving utensil sizes, availability, visibility and convenience, and television and other screen viewing while eating. Furthermore, Bandura's social cognitive model is particularly helpful in planning interventions by identifying four key processes are important in learning and adopting new behaviors: Attention, Retention, Production, and Motivation.[115] These four processes guide the macro and micro development and implementation of all components of the overall program.

7.2. Description of the Intervention

7.2.1 Community-Based Team Sports

We will form after school and summer team sports programs specifically for overweight and obese 7-11 year old children at 4-6 community center sites (Boys and Girls Clubs and Parks and Rec) in East Palo Alto, Menlo Park, and Redwood City, CA. Our community center/after school program partners and the Positive Coaching Alliance, Team Up for Youth (Coaching Corps), and the Stanford Athletic Department, have agreed to collaborate with us to deliver the team sports program at their sites. The sports program will provide regular opportunities for sustained bouts of moderate-to-vigorous activity and participation on a team. Children will not be forced or coerced to attend the sports program, as children will be able to participate in as many or few of the days as they wish and to attend any one or more after-school sites. Our experience to date suggests that the sports program will be sufficiently motivating to produce high levels of participation over the entire length of the intervention. Conducting the sports program at community centers and schools eliminates a substantial transportation barrier to attendance because of an existing transportation network for community children. Both attendance records and coach reports from our feasibility and pilot studies, described above, confirmed high levels of attendance and participation. Child and parent reports suggested that a supportive environment with emphasis on teamwork and respect was a motivating factor. Based on our experience to date, we will offer the sport program five days per

week, excluding holidays. We have designed a curriculum with in collaboration with our Team Sports Advisory Group, currently including representatives from Boys and Girls Clubs of the Peninsula, Stanford Athletic Department, Team-Up for Youth/Coaching Corps, Positive Coaching Alliance, Bay Area Women's Sports Initiative, FitKids, Performance Science Training Institute, and PlayRugby USA. Our daily team sports activity sessions themselves will approximate about 1 hour but, by partnering with the existing after school programs, most children will attend for about 2-3 hours, including homework and tutoring periods (we have learned that this is a motivating feature for parents and schools).

The team sports intervention will continue year-round. This has several important advantages: (1) it provides opportunities for children to continue their physical activity routine without a summer hiatus, and an accompanying relapse of inactivity and sedentary behaviors, (2) it creates a consistent year-round routine schedule for kids and families, (3) there are few affordable summer camps/activities available for children in low-income communities and parents are eager to find ways to keep their kids busy, (4) if parents are fortunate enough to find other summer programs or summer school for their children they usually follow a school-day schedule but leave the after school hours open, and (5) finding supervision for children during the after school hours (while parents/guardians may be working) is a challenge for parents year-round, not just during the school year. In our prior studies of year-round after school programs (e.g., GEMS, ECHALE), we find that overall participation rates do drop off during the summer due to children who leave the area for blocks of time. For the majority of children who remain in the area, however, enthusiasm stays extremely high, and parents/guardians are very excited to have a low-cost (free in our case), enjoyable, enriching and supervised program for their children over the summer. Before these experiences we did not know what to expect during the summer months. But the success to date reinforces our beliefs that the potential benefits to weight control from year-round physical activity, and the practical program implementation benefits, outweigh concerns about continuing the team sports program over the summer.

Based on the results of our formative and Pilot studies we have identified four main sports that will be the focus over four, 3-month seasons, soccer, basketball, flag football and lacrosse. If 3-month seasons prove to be too long we have the option of adding additional sports. We are also arranging to have athletes from various Stanford Varsity sports introduce a variety of other sports during special integrated mini-seasons. Sports were selected based on the ability to involve children with limited or no prior sports experience and ability to teach to children with varying skill and experience levels. We found these sports are easy to learn for children of various abilities and ages, produces high levels of enjoyment for both boys and girls (we were worried that flag football would be less appealing to girls but this was clearly not the case) and promote substantial doses of moderate-to-vigorous physical activity during practices and games. In contrast, we also tried track and field activities but did not find the same level of enthusiasm. Consistent with our hypotheses regarding the appeal of team sports, our coaches described a noticeably less effort from children when learning and playing non-team sports. The children were less engaged in the activities.

Daily 1 to 1.5 hour activity sessions will include warm-up, skills and drills and scrimmages. A lead coach at each site will be supported by 2-6 Stanford undergraduate interns at each practice. All coaches will be trained on positive coaching techniques and promotion of growth mindsets in participants. An emphasis is placed on time spent in movement and game-play which promotes higher intensity physical activity and breaking up participants into smaller groups favoring more participation and one-on-one attention.

In addition, we will include an innovation to emphasize the importance of hard work leading to improved performance. Feedback on skills improvement is motivating and consistent with the growth mindset framework. As a result, we are providing objective feedback on skills acquisition. The skills challenge will be conducted periodically throughout each season and coaches will meet with players one-on-one to set goals for the next skills challenge. Performance is quantified and provided back to participants in real time. This is proving successful and motivating in our Pilot study.

One area of attention going into the Pilot study was the feasibility to handle the 7-11 age-span in the same sports sessions. We found that the activities we designed were engaging across the entire age range and proved feasible to implement. This may be helped by the population we are targeting. The majority of our overweight and obese children have not participated in sports to any significant extent in their recent pasts, somewhat leveling the playing field (so to speak). In addition, our emphasis on growth mindset encourages more individualized attention and a focus on effort to improving one's own skills rather than constant comparisons with the rest of the group, even within the team context. In addition, much broader age ranges are common in the after school programs and sports teams run at the same sites by our community partners. Therefore we do not find it necessary to break children into groups by age. However, we do break up into smaller groups to increase participation, intensity of effort and more one-on-one attention. Therefore, if physical disparities start to manifest as problems over the course of the study we know we can perform drills and games in subgroups defined by size and skill level.

We will recruit our after school sports coaches from the local community and also involve Stanford University undergraduate and graduate students and athletes as volunteer coaches and homework tutors. Training for coaches will be assisted by three of our partners, the Positive Coaching Alliance, the Team Up for Youth Coaching Corps program, and the Stanford Athletic Department. Sports equipment and uniforms will be provided to participants. We put particular emphasis on motivational processes[115] and apply the principles derived from Mark Lepper and colleagues' work on perceived choice and control, personalization, contextualization, challenge, curiosity and mastery that have been demonstrated to enhance intrinsic motivation, greater persistence, better performance, and higher satisfaction in children.[105, 117, 118] These are applied in the designs of the daily practice protocols, specific drills and games, and highlighted in our training of coaches. Our results to date strongly support this approach.[8]

We will also include a feature of objective performance feedback for coaches. Feedback has proven to be a particularly salient motivator to improve performance across many different learning and performance contexts. We have adapted the SOFIT direct observation system for use as a training and feedback tool for our coaches. We added a higher level of moderate-to-vigorous activity to the SOFIT activity intensity scale and coding for the amount of time spent in time management activities (aka instruction time, which we aimed to minimize in our sessions) and the amount of time spent in fitness, skills and game play activities (which we aimed to maximize in or sessions). Specific goals are set for each of these parameters (≥ 55% of time in MVPA, < 25% of time in group management, and ≥ 65% of time in fitness, skills and game playing). Coaches are trained to code the three parameters using videotapes and then observe sessions either directly or on videotape. Coaches can use this feedback and their training to alter their performance and increase the amount and intensity of physical activity while minimizing instruction time. In addition to motivating coaches to improve their session management, we will use this as a process measure to monitor intervention fidelity. We are also in the process of developing a measure of growth mindset-consistent coaching behaviors that can be added to these SOFIT-based direct observations.

What about attempting to improve diet and decrease sedentary behaviors? The most obvious effect of the team sports intervention is increased physical activity. However, an attractive after school program also removes children from in front of their television and video game screens (including the accompanying eating and advertising), as well as their refrigerators, junk food and fast food, during the largest discretionary block of time during their day. In addition, typical after school snacking will be replaced with low fat fruit and vegetable snacks and water during the sports activities. In Stanford GEMS, Stanford ECHALE, and our team sports feasibility and pilot studies, we found that these snacks are desirable to children when offered within the positive context of the dance classes or sports, and presented attractively (e.g., customized water bottles) and by an enthusiastic dance teacher or coach. Laboratory studies suggest that such an intervention may also increase preferences for these healthful choices.[119]

7.2.2 Home-Based Environmental Intervention to Reduce Portion Size

Our home-based environmental intervention to reduce portion size will be the first to be introduced to families as part of the home intervention. This was decided based on our experience in an ongoing home-based environmental intervention to reduce screen time and portion size in obese children. During home visits during the first three months, the home interventionist will assess the current home environment by measuring and completing an inventory of existing glasses, dinnerware and serving utensils. They will then help families select glasses, dinnerware and serving utensils from our samples and catalog, and based on our Phase 1 Pilot studies of optimal designs for promoting illusions of more food on a plate. Families will receive a full set of new glasses, mugs, dinner plates, salad plates, salad/soup/cereal bowls, fruit/desert bowls and serving utensils as needed according to our protocol, to replace their current sets (2 place settings per member of the household). Families will be instructed to be ready to pack-up and replace all their existing glasses, dinnerware and serving utensils at the next visit. Our goal is to provide taller thinner glasses and new dinnerware that represents a 25% to 50% reduction in volume and/or surface area compared to their prior glasses and dinnerware. We found this to be easily feasible in our past feasibility and pilot studies. After many visits to department stores, online catalogues, and measuring the glasses, dinnerware and utensils in the homes of participants in our community-based prevention studies, we have identified the following "typical" sizes and study goal criteria sizes (based on availability of options that would be acceptable):

Table 7.1. Typical and Goal Dishware sizes

	Typical sizes	**Our study criteria/intervention sizes**
Glasses	16-20 oz.	≤ 10 oz. and external height ≥ 2 x internal diameter
Coffee/tea mug	10-16 oz.	≤ 8 oz. and external height ≥ 2 x internal diameter
Dinner plate	≥ 10" diameter	≤ 9" diameter
Salad plate	7-9" diameter	≤ 7" diameter
Bread and butter plate	6-7" diameter	≤ 6" diameter
Salad/soup/cereal bowls	16-24 oz.	≤ 12 oz. and external diameter ≤ 6"
Serving Spoons	≥ 3 oz. (~90ml)	Tablespoon (.5 oz. ~ 15ml)

At the next home visit, the mentor/interventionist will deliver all the new glasses, dinnerware, and serving spoons selected by the family at the first home visit to replace their existing sets (and if relevant, a new set of teaspoons and salad forks). Old glasses, dinnerware, serving utensils, tablespoons, soup spoons and dinner forks will be carefully packed into boxes for storage. The interventionist will bring all necessary packing materials. We initially encouraged families to donate their old dinnerware to a non-profit but found few families willing to do this before the end of the study. We will store the old dinnerware for them for the duration of the study. Our experience to date suggests that the excitement and novelty of receiving all new glasses and dinnerware is highly motivating and, in almost all families, overshadows any lingering disappointment about storing their old property.

For the few families that resist our taking away their old dishware (e.g., the designer plates of family gifts) we help them pack and tightly seal it in boxes to store somewhere difficult to access in their home. Some parents have been particularly reluctant to part with the large coffee mugs they use daily. In these cases parents may be left with one coffee mug each, but only if they insist. We are providing new mugs. Other things we have learned not to take: Anything of sentimental or monetary value that they do not want us to take may be packed and stored in their home; China

only used for special occasions; Bread and butter plates, very small bowls and small glasses may be left if they are smaller than our threshold measures; Water bottles and thermos bottles.

During the design of the intervention we anticipated difficulties in implementing the home-based intervention for families where the child lives in multiple households. For these families we try to gain full participation of all households but we also use a modified intervention to implement in secondary households when the child's time is primarily spent in one household (consumes four or fewer meals per week in a second, third or more households, including parent, grandparents or other caregivers). This has proven to be a successful strategy for this situation and has made it possible for more families to participate.

The initial trade-out of dishware can occur over 2 home visits but at all subsequent visits interventionists continue to monitor dishware use and provide positive reinforcement and continued and/or recurrent instruction and modeling to increase efficacy beliefs and promote maintenance or additional attempts to make environmental changes.[115, 116] At least once a year, the interventionist will (1) Assess the home environment completing a repeat inventory of glasses, dinnerware and serving utensils, to compare with prior visits, and (2) Provide new matching replacement glasses, dinnerware, and utensils as needed (families will be instructed to call the project toll-free hotline/email to request replacements for lost or broken items – we find this occurs readily). If families are no longer using the study-supplied glasses, dinnerware, or utensils, or others that meet our study criteria (e.g., because they have retrieved their old ones or acquired new ones) the interventionist will follow a structured counseling protocol to help them start again.

7.2.3 Home-Based Environmental and Behavioral Intervention to Reduce Screen Time

Our screen time reduction intervention is based on the same model used in Stanford GEMS, Stanford ECHALE, our collaborative screen time reduction study in Buffalo, and an ongoing home-based environmental intervention to reduce screen time and portion size in obese children. We are finalizing the intervention protocols as we complete the Pilot study. It will be able to be delivered in smaller modules over 6-9 months to allow families to choose the order of behaviors they wish to focus on. It will start with an introduction to "brainology" and a growth mindset, based on Carol Dweck's intervention studies to improve math performance in girls. Children and their parents have been particularly enthusiastic about this framing in our Pilot study in part, we believe, because it presents a fresh perspective compared to their expectation of being scolded for their behavioral lapses. The intervention then focuses on building skills and competence for two main screen time reduction strategies, reducing eating while watching screens and reducing total screen time.

The interventionist schedules visits to meet with the parent(s) and participating child (usually afternoons, evenings or weekends) and other family/household members, particularly siblings, are encouraged to attend. The interventionist acts as a behavior change partner for the participating child and a parenting counselor for the parent(s). While occasional families avoid the visits, almost all families embrace their home visitor and welcome them into their home and family. Our home-based interventionists in past and ongoing studies have reported feeling tremendously gratified about the perceived impacts they are making, going far beyond improving health behaviors. Parents have attributed their children's improved school performance, better behavior, and greater sense of personal worth and responsibility to the visits. In addition, over the several years we have observed increased acceptance, and even desire, for home visits and home-based counseling. Based on testimonial comments we believe this may be due to the high prevalence of home and personal makeover reality television shows (e.g., Super Nanny) in which a subjects make dramatic changes in their lifestyles with the help of a home visitor.

Our screen time reduction intervention approach has been developed over multiple prior studies to include three primary approaches:

(*1) Non-Selectively Decreasing Screen Time,* by (a) budgeting total weekly hours of screen time – e.g., using electronic TV time managers; and (b) physically reducing access to television sets, VCRs/DVDs and video game players and computers (e.g., removing TV sets from home, kitchens and/or children's bedrooms, moving TV sets into cabinets and away from central focal point locations of rooms, hiding remote controls).

(2) Selectively Decreasing Screen Time, by (a) limiting screen time by day or time (e.g., not until homework is completed, not on school nights); (b) limiting screen time based on content (e.g., violence or sexually explicit content as indicated by ratings, limited to PBS, Disney and Nickelodeon, only videotapes/DVDs, no cable); and (c) limiting screen time based upon context/setting (e.g., only with a parent present, no TV during meals, not allowed to use TV set in kitchen, parents' bedroom or living room).

(3) Displacing Screen time with Other Activities, by participating in family, school or community, athletic, or other activities, classes or teams after school, in the evenings and on weekends, when most viewing occurs. The team sports intervention is an example of this.

The above methods are applied throughout home-based and occasional phone counseling lessons. Activities are designed to include multiple levels of achievement, challenge, fantasy, personalization, choice, and perceived control to maximize intrinsic motivation for continued participation.[105, 117, 118, 120, 121] Early lessons are designed to increase awareness of current media use and build motivation to change television, videotape and video game habits, among the children themselves as well as their parents/guardians and other family/household members. These lessons include self-monitoring, reviewing favorite activities, becoming aware of the impact of media on their family, and becoming aware of questionable media content. Those lessons will be followed by a 2-week TV-Turnoff,[122] during which families attempt to watch no television or videotapes/DVDs and play no video or computer games for 14 days. The turnoff is accompanied by activities to promote positive outcome expectancies and greater perceived self-efficacy for reduced screen time. Phone calls occur as scripted check-in/problem solving counseling sessions during the turnoff. Following the turnoff, lessons 3 and 4 introduce and establish the budgeting process that will continue for the rest of the intervention. The home interventionists will help families choose appropriate starting budgets and help them install BOB electronic TV time managers (on as many televisions as possible in each home).[4, 37, 49] The BOB TV time managers control power to the television set and monitor viewing times with a Personal Identification Number (PIN) for each member of the family. Parents set weekly time budgets for their child(ren), and can block use during certain times of the day or week. When the weekly budget expires, the TV set turns off and cannot be turned on again with that PIN until the next week. The children select their own PIN ("secret code"). Parents and other caregivers will be helped with contingency management skills, including selection of appropriate reward and reinforcement schedules.

We also work with parents to set block out times so the TV cannot be turned on during meal times (currently a 2 hour block in the morning before school and at the usual dinner time for the child, as selected by the family) or at bedtime (as many parents agree TV is interfering with sleep). Families will also receive kits to help them control their screen time, with reminder placards and “table tents” for children to assemble and decorate to personalize them (increasing intrinsic motivation) and to place over and/or on top of each television set and computer monitor as a reminder. We have used this method with success in prior studies of reducing overall screen time in this age group.[4, 36] Subsequent home visits and phone calls are used to check-in with budget progress/success and help problem solve barriers. In addition, they will introduce “Intelligent viewing,” or being more selective about what you watch or play (instead of whatever happens to be on), as a strategy to stay under budget. Screen time reduction can also be integrated into visits for other modules to promote long-term maintenance of budgeting (or to restart budgeting if it has lapsed).

7.2.4. Family-Based Behavioral Counseling for Diet and Activity Change

The family-based behavioral counseling intervention is designed to split into three 6-9 month modules: reducing energy intake, increasing physical activity, and problem solving. They can be delivered in any order, along with the screen time reduction intervention, depending on the order preferences of the family. Based on our experience to date in our Phase 1 pilot study, we believe this component can substantially improve behavior change and address a perceived need of the participating families for behavior-relevant knowledge. In our pilot studies we have found families with overweight children possess few skills to achieve the diet, activity and weight goals that they aspire to. Like the screen time reduction intervention, it will start with an introduction (or a "booster" if not the first module to be delivered) to "brainology" and a growth mindset, based on Carol Dweck's intervention studies to improve math performance in girls.

The intervention content is adapted directly from the Stanford Pediatric Weight Control Program individual family counseling version used in the clinical setting. The diet module includes: Learning the traffic light food categories (based on energy density) to help them count and change their intake; self-monitoring (or journaling) according to the traffic light colors with a personal behavior journal; setting goals to reduce red light foods; reciprocal contracting with parents/guardians, and instruction for parents about the appropriate use of rewards to build intrinsic motivation. The physical activity module similarly includes: monitoring (journaling) activity and earning "activity points," setting goals to increase activity points, earning a pedometer to set new goals, reciprocal contracting with parents/guardians, and instruction for parents about the appropriate use of rewards to build intrinsic motivation. The problem solving module includes: limit setting, modeling behavior, practice to promote enactive mastery, role-playing to overcome barriers, enlisting social support, and general problem solving, especially with regard to fast food, holidays, difficult family members, and maintenance skills.

7.2.5 Primary Care Counseling Intervention

The primary care counseling intervention exists in parallel with the after-school sports intervention and home/family-based intervention components, throughout the entire duration of the study. Consistent with making our MMM intervention model practical and generalizable, our primary care counseling intervention is designed to be easily incorporated into current primary care practice. An important design feature is establishing a partnership link between the medical care setting and the community centers/after school programs -- addressing a desire voiced by many primary care providers for more community treatment resources to refer to. This does not have to change their existing referral patterns for subspecialty evaluation and management but establishes a new model for treatment at their disposal.

To assist primary care providers with their assessment of overweight and obese children we are supplying simple and quick tools to help them assess patients and identify those most appropriate for referral to our study. Then, to facilitate subsequent counseling and further integrate them with the community- and home-based interventions, participants randomized to the MMM intervention will receive "progress reports" every three months, that they may take to visits with their primary care providers/clinics. These reports will be personalized to the specific goals and performance of each child and family reflecting their after-school sports intervention participation and their home/family-based interventions. These will be faxed to those providers and clinics identified by participants as their source of primary care. They are accompanied by a Structured Encounter Form that will lead them, step-by-step through behavioral counseling interactions specifically tied to their patients' progress reports. This serves to further tie the providers to the ongoing community intervention and provides an opportunity to reinforce the messages and changes that are being implemented outside their clinic or office. We use SEFs because they been found to be particularly easy and effective

strategy for integrating new skills into practice.[101] We are currently finalizing the design of the SEFs. We will not make recommendations to participants about their frequency of visits to their primary care source as we wish to leave that up to the participants and their primary care providers. We have found a tremendous diversity of standard intervals recommended for follow-up for weight issues among primary care providers.

In addition to the "progress reports," we send the results of annually scheduled metabolic studies and blood pressure to identified primary care sources for all participants, those randomized to the MMM intervention as well as those randomized to the enhanced standard care/health education intervention.

7.3. Process Measures

We assess the success of intervention implementation throughout each participant's participation in the trial, to describe intervention exposure and explain potential variations in individual responses. This includes attendance and participation rates for each element of the experimental intervention, observations of team sports (direct observation/checklists) and home visits (checklists) to estimate the fidelity of intervention delivery, home observations of the extent of adoption and maintenance of changes in dishware, and installation and use of electronic TV time managers, achievement of goals, primary care visits and use of progress reports and SEFs. Only intervention staff (unblinded) will collect implementation data, to maintain data collector blinding.

Table 7.2. Process measures

Fidelity: *The extent to which the intervention is delivered as intended; quality of the intervention; how well an intervention is being implemented compared to its original design; could include, but not limited to, content & quality of messages, adherence to protocol, and intervention staff skill/training/certification.*				
Fidelity	**Fidelity Construct**	**Data Collection Method**	**Completed By**	**Timing of Data Collection**
After-School Sports	Quality of activities delivered	SOFIT Class Observation	Coaches	Weekly to monthly
		Coaches Checklist	Coaches	Every session
Home Visits	Quality of intervention delivery	Home Visit Checklist: content of lessons delivered at home or via telephone	Home Advisors	Every home or telephone visit
Primary Care Visits	Delivery of lab results and progress reports to primary care	Fax records	Intervention Staff	Continuous
	Delivery of progress reports (SEFs) to primary care	Document dates materials are faxed	Intervention Staff	Continuous

	Delivery of lab reports to participants	Mailing records	Intervention Staff	Continuous
	Delivery of progress reports to participants	Mailing reports	Intervention Staff	Continuous
Health Education	family fun nights quality	FFN checklist	Intervention staff	During FFN
	Home visit quality	Home Visit Checklist: content of lessons delivered at home or via telephone	Home Advisors	Every home or telephone visit
Dose Delivered: *The amount of intervention that was delivered; could include, but not limited to, number and length of sessions implemented*				
Dose Delivered	**Dose Delivered Construct**	**Data Collection Method**	**Completed By**	**Timing of Data Collection**
After-school sports	Number of sessions	Attendance form	Coaches	Each session
Home visits	Number and content of home visits and telephone visits conducted	Home Visit Checklist	Home Advisors	After home or telephone visit
	Delivery of dishware	Home Visit Checklist	Home Advisors	After appropriate home visit
	Installation of TV time managers (and number)	Home Visit Checklist	Home Advisors	After appropriate home visit
Primary care	Number of primary care visits	Participant report	Home advisors	At home or telephone visits
Health Education	Number of parent newsletters mailed	Number of mailed letters and returned undelivered	Intervention staff	Continuous
	Number of child newsletters mailed	Number of mailed letters and returned undelivered	Intervention staff	Continuous
	Number of family fun nights conducted	FFN checklist	Intervention staff	At FFN
	Number of home visits conducted	Home visit checklist: number of home or	Home advisors	Every home or telephone visit

		telephone visits		
Dose Received: *The amount of intervention that was received; could include, but not limited to, participant engagement, and intervention messages or materials received*				
Dose Received	**Dose Received Construct**	**Data Collection Method**	**Completed By**	**Timing of Data Collection**
After-School Sports	Attendance	Attendance form	Coaches	Every session
	Improved skills	Skills challenge	Coaches	Weekly to monthly
Home Visits	Number and content of home and telephone visits completed	Home Visit Checklist	Home Advisors	After home visit
	Number of days recorded in participant journals	Home Visit Checklist	Home Advisors	At each home visit
	Achievement rates of eating, activity and sedentary behavior goals	Home Visit Checklist	Home Advisors	At each home visit
	Dishware in use in home	Home Visit Checklist	Home Advisors	At each home visit
	Percent reduction in the size of dishware	Direct measurement of dishware	Home advisor	After appropriate home visit
	TV time managers in use	Home Visit Checklist	Home Advisors	At each home visit
	Number of family members participating in home visit	Home Visit Checklist	Home Advisors	At each home visit
Primary Care Visits	Number of visits to primary care clinic (reported by participant)	Participant report	Home advisor	At home visits
	Use of feedback/progress report forms during primary care visit (reported by participants)	Participant report	Home advisor	At home visits
Health Education	Number of parent and child newsletters completed	Number of mailed letters and number returned undelivered.	Intervention staff	Continuous

		Number of mail-back activities received.		
	Number of home and telephone visits conducted	Home visit checklist	Home Advisors	After Home or telephone visit
	Number of Family Fun Nights attended	Attendance form	Intervention staff	During FFN

7.4. Unblinded Process Measures

We have identified a modest selection of process variables that we will monitor (as distributions) in treatment groups as a whole during the study, to help implement the interventions. While some have similar names in the two treatment groups, each is specific only to its own intervention. Thus, the two groups cannot be compared on any of these variables.

MMM intervention group:
- After school intervention:
  - Attendance rates at after school activities
- Home/family intervention:
  - Number of home visits/telephone visits
  - Behavior journal completion rates
  - Achievement rates of eating, activity, and sedentary behavior goals
  - Dishware delivery and use rates
  - Electronic TV Time manager delivery and use rates
- Primary Care intervention:
  - Number of primary care visits
  - Number of structured encounter forms (SEFs) sent to primary care providers

Control standard care/Health Education intervention group:
- Family intervention:
  - Attendance rates at family fun nights
  - Child newsletters delivery rates
  - Parent newsletters delivery rates
- Home visits:
  - Number of home visits/telephone visits

8. CONTROL CONDITION

The choice of an appropriate control group for our experimental treatment procedures is not one we make lightly. First and foremost, we believe the evaluation of the entire MMM intervention is the research question of greatest clinical, practical and policy importance.[123] Second, we also believe that an untreated control condition is not warranted in children at risk for significant physiological, psychological and social morbidity. Even if one does not agree, however, there are practical reasons as well, which are particularly salient when working with an racially/ethnically- and socioeconomically-diverse sample of participants. In times past, the rights of ethnic minorities have occasionally been ignored and trampled upon in the pursuit of questionable scientific objectives. As a result, many disadvantaged groups, and many people in general, have come to view the scientific enterprise with suspicion. Failure to consider and attend to the negative attitudes towards science that exist in ethnic minority and low-income communities will seriously jeopardize the ability of any research team to conduct a successful trial. Our experience convinces us that a no treatment control condition would likely deter recruitment and facilitate considerable contamination, or result in resentful demoralization or compensatory rivalry, serious threats to internal validity.[124] A waiting list control condition would be problematic for similar reasons and is not feasible. We cannot expect families to wait 36-months to receive treatment. Our choice, instead, contains certain "active" ingredients, such as health/nutrition education, which may influence behavior, but these ingredients differ from the conceptually relevant ingredients of concern to us.[125, 126]

Our comparison condition is an enhanced standard care/health education intervention. After meeting eligibility criteria and completing baseline measures, participants are randomized to either the experimental MMM intervention described above or to an enhanced standard care/health education comparison intervention. The enhanced standard care intervention includes notification of primary care providers about their metabolic measures and blood pressure (but not "progress reports") and standard follow-up determined with their primary care provider, and state-of-the-art information-based health education. The health education components include periodic quarterly or semi-annual home visits with a home interventionist for education about nutrition, monthly health education newsletters for children and for parents/guardians, and a series of quarterly evening health lectures and "Family Fun Nights." These evening events are held at the community centers or school sites on weeknights to facilitate entire-family attendance. Health lectures will be led by volunteers from the American Heart Association, the American Diabetes Association and our own research team. Bilingual Family Fun Nights have been developed for our ongoing trials to involve all age groups in games relating to health and nutrition knowledge. They can be engaging social events. Unfortunately, our experience is that attendance will be limited but it is what participants and community representatives say they want and expect in terms of health education. Therefore we believe they still provide an important role in meeting expectations for responsiveness. The newsletters utilize standard educational materials from federal health agencies (USDA, CDC), health organizations (AHA, ACS, ADA), professional organizations (AAP, ADA) and our own research team. An important purpose of including this health education component is to address the expectations of participants who were referred to/joined a study for overweight and obese children. They are expecting some intervention related to weight control. This comparison intervention model worked well at keeping participants engaged in trials throughout 2 years, in Stanford GEMS, Stanford GAMES and Stanford ECHALE, without evidence of resentful demoralization or compensatory rivalry.[124] Although this comparison intervention contains ingredients that may have specific, albeit limited, effects on behaviors influencing weight gain, they are very different from the mechanisms operationalized in the experimental intervention.

Finally, monetary incentives will be included to enhance compliance with measurement protocols in both groups, and may have effects on behavior. The monitoring and incentive schedules employed for our experimental treatment procedures will also be used to sustain

participation of those assigned to our active placebo condition. Thus, these “non-specific” and “specific” effects will be equated for across the MMM intervention and active placebo control groups.

9. MEASUREMENTS

9.1. Methods

Our research team has extensive experience in longitudinal, clinical and community-based, data collection. Data collection is performed in a clinic, community or home setting at all time points, baseline, 12-, 24- and 36-months, by trained and certified, bilingual (English and Spanish) research assistants, *blinded t*o experimental assignment. Assessment appointments are scheduled to correspond as closely as possible to a ± 4-week window around the target date (note: use of trajectories of BMI change in the primary analysis, described below, minimize effects of scheduling difficulties, if they cannot be avoided). Data collectors are trained by the investigators and, for common consortium measures, by the RCU according to standardized protocols. Data collectors are required to demonstrate high inter- and intra-rater reliability prior to actual data collection. At each assessment time point, a random 10% sample undergoes repeat height & weight, skinfold thickness, and waist circumference measures to estimate test-retest and inter-rater reliability. Data are directly entered into laptop computers using customized software. We chose the following measurement schedule to satisfactorily model changes over time while minimizing potential "fatigue" in subjects resulting in poor quality participation.

It is important to both maintain internal validity and also maximize generalizability. Therefore, we have chosen measures that can be feasibly, reliably and validly assessed in clinic, community and home settings. Of course, this also means excluding other measures. We believe this trade-off is well worth the potential benefits of greater generalizability and improved participant retention.

9.1.1. Primary Outcome and Other Anthropometric Variables*

9.1.1.1. Primary Outcome

Background and Rationale

The measure used as the primary outcome variable of all four COPTR trials is body mass index (BMI). BMI assesses body weight adjusted for height and is correlated with percent body fat as assessed by dual energy x-ray absorptiometry (Bray, DeLany, Harsha, Volaufova, & Champagne, 2001; Daniels, Khoury, & Morrison, 1997; Dezenberg, Nagy, Gower, Johnson, & Goran, 1999; Pietrobelli et al., 1998). When calculated using measured anthropometrics BMI is highly reliable. BMI has demonstrated clinical validity in its associations with type 2 diabetes mellitus (Pinhas-Hamiel et al., 1996; Scott, Smith, Cradock, & Pihoker, 1997) , hyperinsulinemia (Freedman, Dietz, Srinivasan, & Berenson, 1999), blood pressure and hypertension (Daniels, Khoury, & Morrison, 1997; Dwyer et al., 1998; Freedman, Dietz, Srinivasan, & Berenson, 1999), adverse lipoprotein profiles (Dwyer et al., 1998; Freedman et al., 1999; Teixeira, Sardinha, Going, & Lohman, 2001) and early atherosclerotic lesions (Berenson et al., 1998; Mcgill et al., 1995) among children and adolescents. Importantly, BMI can be assessed easily in clinical and public health settings and is generally accepted and well understood.

Objective

The objective of the BMI measures is to provide a precise and accurate measure of the impact of the intervention on relevant aspects of body size in the children studied in COPTR.

Methods
All consented index children in the COPTR study have weight and height measured at the beginning and end of the intervention (36 months) and at two common interim time points (12 and 24 months). All baseline anthropometric data will be collected prior to randomization. Weight and height are measured with the participant in light clothing without shoes. Weight is measured to the nearest 0.1 kg using research precision grade, calibrated, digital scales and height is measured to the nearest 0.1 cm using a free-standing or wall mounted stadiometer. BMI is calculated as weight in kilograms divided by the square of height in meters.

All height and weight measurements are collected by trained and certified staff. COPTR will use a "train the trainer" model. Each field center will designate one or more "Master Trainers" who participate in a central training organized by the RCU at the University of North Carolina at Chapel Hill on April 16-18, 2012. These Master Trainers are responsible for training and certifying the data collection staff at their center.

9.1.1.2. Other Anthropometric Secondary Outcomes

Anthropometric secondary outcomes differ by site as detailed in Table 9.1. Variables measured in the index child at all sites include waist circumference and triceps skinfold. All sites are measuring height and weight in at least one adult family member of the index child and some sites are measuring siblings. Secondary outcomes that will be calculated from anthropometry in at least one site include BMI z-score, waist-to-height ratio (WtHR), and percent body fat.

Table 9.1 Anthropometric Common Measures by Research Center

Anthropometric Measure	**Case**	**Minnesota**	**Stanford**	**Vanderbilt**
Index Child				
Weight	x	x	x	x
Height	x	x	x	x
Waist circumference	x	x	x	x
Triceps skinfolds	x	x	x	x
Other Children				
Weight	--	x*	x†	--
Height	--	x*	x†	--
Waist circumference	--	--	x†	--
Triceps skinfolds	--	--	x†	--
Other Adults				
Weight	x	x*	x	x
Height	x	x*	x	x
Waist circumference	--	--	x	x
Triceps skinfolds	--	--	--	x

* Minnesota: All children and adults in household.
† Stanford: Only study eligible children

Background and Rationale
BMI z-scores provide a method for evaluating the weight status of children adjusted for age and gender. The measure is commonly used in clinical practice to track body size trajectory. However, several authors have cautioned against the use of BMI z-scores for research using longitudinal

designs citing concerns that their use could result in spurious differences between groups (Berkey & Colditz, 2007; Cole, Faith, Pietrobelli, & Heo, 2005). One reason for this problem is that children at the extreme ends of the BMI distribution require substantially greater changes in weight than their thinner counterparts for the same change in z-score. Also because the BMI z-score curves were constructed using only data between the 3rd and 97th percentiles, the CDC recommends extreme caution when using the growth curves outside this range (Kuczmarski et al., 2000). Finally, Berkey et al. noted that the difference between z-scores reflect larger differences in BMI in older compared to younger children. For these reasons the COPTR investigators have chosen to study BMI z-score as a secondary rather than a primary outcome.

Abdominal adiposity is associated with metabolic risk factors in children (Caprio et al., 1995; Caprio et al., 1996; Freedman et al., 1987; Freedman, Srinivasan, Harsha, Webber, & Berenson, 1989) although evidence to date suggests that anthropometric measures tend to only moderately predict visceral fat (Goran, 1998a; Goran1998b). Waist circumference is a feasible non-invasive measure of abdominal fatness for community-based assessments of children. It has also been shown to be sensitive to change in response to prevention interventions (Robinson, 1999).

Waist-to-height ratio (WtHR) is a simple index that has recently received increased interest from investigators (Browning, Hsieh, & Ashwell, 2010). After the age of four years, waist and height appear to simultaneously increase during childhood and adolescence (Kahn, Imperatore, & Cheng, 2005). Thus, WtHR could provide a practical estimate of adiposity that could be consistently applied to a wide range of age groups. Recently Browning et al. (2010) published a systematic review of waist to height ratio as a screening tool for cardiovascular and diabetes-related outcomes. In their examination of 13 cross-sectional studies in children they found that waist-to-height ratio compared favorably with waist circumference and BMI. In a cross-sectional study of 1,511 youth 8 to 17 years of age McMurray et al. (2010) found that waist circumference performed well as a predictor of insulin resistance in boys but not girls. Better performance was observed when waist circumference was divided by height, producing an index that was highly associated with insulin resistance in both genders and over a range of ages. Kahn et al. (2005) and Savva et al. (2000) have suggested a WtHR cut point of 0.49 to distinguish high and low levels of risk, however, McMurray et al. (2010) suggest that a WtHR of 0.54 may result in fewer misclassifications. WtHR can also be analyzed in the continuous form. COPTR can provide an opportunity to further evaluate this index using both cross-sectional and longitudinal designs.

Triceps skinfold thickness is a measure of subcutaneous fat and is a component of equations used to predict percent body fat. COPTR investigators are using data from the NHANES study to develop a prediction equation for percent body fat that uses triceps skinfold along with other anthropometric variables collected in COPTR (height, weight and waist circumference) together with demographic variables to predict percent body fat (see section 4.8. in RCU protocol). Equations were developed in children in the age ranges being studied by Case Western and Stanford. Preliminary work indicates that this equation has an R^2 of over 0.8. Unfortunately estimates of percent body fat from DEXA are not available in children less than 8 years of age in NHANES. Therefore Vanderbilt and Minnesota will estimate percent body fat in younger children in their study using the prediction equation created by Dezenberg (1999) (R^2=0.95 as compared to DEXA, Model SEE=0.46) using data from White and African American 4 to 11 year old children. This method has been shown to have higher validity across subgroups than other equations (Goran, Driscoll, Johnson, Nagy, & Hunter, 1996; Slaughter et al., 1988) and has been validated in 3 to 8 year old White and Hispanic children.

Obesity has been shown to cluster in families such that having obese parents increases the risk of obesity in children (Barness, Opitz, & Gilbert-Barness, 2007; Macfarlane, Cleland, Crawford,

Campbell, & Timperio, 2009; Silventoinen, Rokholm, Kaprio, & Sorensen, 2010). This clustering is due to both shared environment and genetic factors. The collection of anthropometric variables in the families of the index children in COPTR provides an opportunity to examine longitudinal changes within families in the family members and to assess any impact of the intervention on family members.

Objective
The anthropometric secondary outcomes are assessed to provide a richer understanding of the changes in body size characteristics associated with the COPTR interventions.

Methods
Waist circumference and triceps skinfolds will be measured at the beginning and end of the intervention (36 months) and at two common interim time points (12 & 24 months). Measurement details have been determined with guidance from the 2007 NHANES anthropometry procedures manual (Centers for Disease Control, 2007, (http://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/manual_an.pdf). Waist is measured to the nearest 0.1 cm just above the uppermost lateral border of the right ilium using a Gulick II tape measure, model 67020.

The triceps skinfold is measured using a Lange skinfold caliper (or a Harpenden caliper if the measurement exceeds capacity of the Lange skinfold caliper) in the midline of the posterior aspect (back) of the arm, over the triceps muscle, at a point midway between the lateral projection of the acromion process of the scapula (shoulder blade) and the inferior margin (bottom) of the olecranon process of the ulna (elbow). Skinfolds are measured to the nearest 0.1 mm.

9.1.2. Common Demographics, Moderators, Mediators and Secondary Outcomes*

9.1.2.1. Demographics, Moderators and Mediators

Background and Rationale
Self-reported information will be collected from COPTR index children and other household members by obtaining responses to written or verbalized questions. Although we refer to "questionnaires", as discussed in the methods section below, several methods are used to collect these data, and only a minority of the data is collected through the use of paper questionnaires. The information obtained is used to describe the study population or as a confounder, mediator, moderator or secondary outcome of intervention effects.

In general, the mediators chosen for measurement are targeted by the intervention, are expected to change as a result of the intervention and to result (directly or indirectly) in change in BMI. In COPTR, each Field Site's intervention is unique and many of the mediator variables are site-specific because they serve as explanatory constructs for the site-specific theoretical model. A moderating variable is defined as a variable that could influence the primary or secondary outcomes because the variable interacts with the intervention to change study outcomes. In other words, the intervention affects people differently, depending on their status on the moderator variable. These variables are evaluated at the beginning and the end of the intervention, and in some cases as interim measurements.

Objective
The purpose is to describe the characteristics of participants, to determine possible mediators and moderators of intervention effects and to study secondary outcomes that are impacted by the intervention.

Methods
The demographic, household, mediators and moderators survey is administered to parents/primary caregivers of the participating child and/or to the participating child. Table 9.2. summarizes the location where the questionnaire will be administered and administration format in each site. To accommodate the sample being studied some sites administer questionnaires in Spanish.

Table 9.3 lists the questions used to collect common questionnaire data and shows which sites are collecting each item. All of the common survey questions are not administered at all Field Sites. The source of the 55 common questions and the responses are listed in Table 9.4. There will be four common measurement time points – baseline, 12 months, 24 months and 36 months. All common data collection will occur between May 2012 and March 2017. All baseline data collection will occur prior to randomization. Measurement data collectors are not intervention staff unless data are collected prior to randomization.

A "train the trainer" model is used to prepare staff to collect questionnaire data. Each Field Site designates two or more "Master Trainers" who participate in central trainings conducted by the RCU at the University of North Carolina at Chapel Hill on April 16-18, 2012. These Master Trainers are responsible for training and certifying the data collection staff at their Field Site. To be certified, Master Trainers attends the central training, reads the protocol and manual of procedures, complete the questionnaire and administer the questionnaire. The data collectors are certified by a Master Trainer who will describe the data collection process, insure that the protocol and manual of procedures are read and observe the questionnaire being administered to a volunteer.

Table 9.2 Characteristics of questionnaire administration by Field Sites

	Field Sites			
	Case Western	**Minnesota**	**Stanford**	**Vanderbilt**
Administration Location	Clinic	Home	Community center, Home, or Clinic	Community center
Administration Format	Interviewer administered	Interviewer administered	Interviewer administered (child) and mix of interviewer and self-administered (parent)	Interviewer administered
Data collection format	Computer	Computer	Paper Computer	Computer
Languages	English	English Spanish	English and Spanish (parents) and English (child)	English only in pilot; English and Spanish in main trial
Respondent	Parent or primary adult caregiver and participating child	Parent or primary adult caregiver	Parent(s) or primary adult caregivers and participating child	Parent or primary adult caregiver

Table 9.3 Questionnaire Common Measures by Field Site

Construct	Item	Case	Minnesota	Stanford	Vanderbilt
Household Configuration	For all children and adults living in your household, please tell me:				
	Gender,	X	X	X	
	Birth date, or age	X	X	X	
	Relationship to the participating child.	X	X	X	
Child's date of birth	Child's date of birth	X	X	X	X
Child Sex	What is this child sex?	X	X	X	X
Child Ethnicity	Is this child Hispanic, Latino/a or of Spanish origin?	X	X	X	X
Child Race	Which of the following best describes your child?	X	X	X	X
Parent Ethnicity	Are you Hispanic, Latino/a or of Spanish origin?	X	X	X	X
Parent Race	Which of the following best describes you?	X	X	X	X
Parent Country of Birth	In what country were you born?		X	X	X
Child Country of Birth	In what country was this child born?		X		X
Years Parent Lived in USA	How many years total have you lived in the United States?		X	X	X
Employment Status	What is your employment status?	X	X	X	X
Marital Status	What is your current marital status?	X	X	X	X
Access to Car	Is there a car that you can use whenever you need to?	X	X		X
Frequency of Speaking English at Home with Family	How often do you speak English at home with your family? (Choose one.)		X	X	
	If you do not always speak in English at home with your family, what languages do you speak the rest of the time?	X	*X*		
WIC	Do you participate in WIC? WIC stands for Women, Infants, and Children, a Federal assistance program.	X	X		X
Food Stamps/ SNAP	Does anyone in your household receive food stamps or SNAP? SNAP stands for Supplemental Nutrition Assistance Program.	X	X	X	X
Unemployment/ Social Security/ Disability	Does anyone in your household receive Unemployment, Social Security, or Disability Benefits?	X	X	X	
Education	What is the highest degree or	X	X	X	X

Construct	Item	Case	Minnesota	Stanford	Vanderbilt
Completed	level of school that you have completed?				
	What is the highest degree or level of school that your child's other parent living in the household or adult caregiver living in the household has completed?	X	X	X	X
Child Care	In a usual week, how much time does this child spend being cared for by someone other than parent/guardian?				
	in your own home		X	X	X
	in someone else's home		X	X	X
	in childcare center/after school program		X	X	X
Household Income	What was your total household income from all sources before taxes last year? By "household", we mean that you should report the combined income of everyone in your home.	X	X	X	X
Child Health Insurance	Is your child covered by a health insurance plan?	X	X	X	
	Which type of plan are they covered by?	X	X	X	
Free or Reduced Price Breakfast or Lunch	Does any child in your household receive free or reduced price breakfast or lunch at school?		X	X	
Maturation Status	Has your daughter started having her menstrual period?	X		X	
	When did she have her first menstrual period?	X		X	
Breastfeeding/ Pregnancy Risk	Did <this child> breastfeed for more than a month?	X	X		X
	How old was <this child> in months when he/she first received a bottle of formula, cow's milk, water, juice, tea, or cereal at least once a day?	X	X		X
	How much did this child weigh at birth?	X	X		X
	Did a doctor say that <you/birth mother> had diabetes when pregnant with <this child>?	X	X		X
	Did a doctor say that <you/birth mother> had hypertension (high blood pressure) when pregnant	X	X		X

Construct	Item	Case	Minnesota	Stanford	Vanderbilt
	with <this child>?				
Food Security	"The food that (I/we) bought just didn't last, and (I/we) didn't have money to get more." Was that often, sometimes, or never true for (you/your household) in the last 12 months?	X[3]	X	X	X
	"I/we couldn't afford to eat balanced meals." Was that often, sometimes, or never true for (you/your household) in the last 12 months?	X[3]	X	X	X
	In the last 12 months, since (date 12 months ago) did (you/you or other adults in your household) ever cut the size of your meals or skip meals because there wasn't enough money for food?	X[3]	X	X	X
	How often did this happen -- almost every month, some months but not every month, or in only 1 or 2 months?	X[3]	X	X	X
	In the last 12 months, did you ever eat less than you felt you should because there wasn't enough money to buy food?	X[3]	X	X	X
	In the last 12 months, were you ever hungry but didn't eat because you couldn't afford enough food?.	X[3]	X	X	X
TV & Media	How many working TVs do you have in your home?	X[1]	X	X	
	Is there a working TV in the room where <this child> sleeps?	X[1]	X	X	X
	Is there a computer in your home?	X[1]	X	X	X
	Is there a computer in the room where <this child> sleeps?	X[1,2]	X	X[2]	X
	Is there a video game player in your home?	X[1]	X	X	
	Is there a video game player in the room where <this child> sleeps?	X[1]	X	X	X
	Do you have Internet access in your home?	X[1]	X		
	On an average WEEK day, how many hours does <this child> watch TV?		X		X
	On an average WEEKEND day,		X		X

Construct	Item	Case	Minnesota	Stanford	Vanderbilt
	how many hours does <this child> watch TV?				
	On an average day, how many hours does <this child> play video or computer games, or use a computer for something that is not school work? (Include activities such as Play Station, Xbox, hand held video games, computer games, and the Internet.)		X		X
Food Norms	During the past seven days, how often did your family eat breakfast together?		X		X
	During the past seven days, how often did your family eat lunch together?		X		X
	During the past seven days, how often did your family eat dinner together?		X		X
Weight Status	How would you classify your own weight?	X	X	X	X
	How would you classify <this child's> current weight?	X	X	X	X

1 – The TV/Media questions for Case are derived from a group of embedded scale questions

2 – Case and Stanford uses the term “desktop” computer in their question.

3—Case questions are embedded into a survey and are not administered as an interview.

Table 9.4 Source and Response Sets of Questionnaire Common Measures

Construct	Item	Response Options	Source
Household Configuration	For all children and adults living in your household, please tell me:		Developed
	Gender,	Male; Female	
	Birth date or age	MMDDYYYY; __ __ yrs	
	Relationship to the participating child.	Mother; Father; Stepmother; Stepfather; Other male CG, (list); Other female CG, (list)	
Child's date of birth	Child's date of birth	MMDDYYY	Developed
Child's sex	What is this child's sex?	Male; Female	HHS data standards (Dorsey & Graham, 2011)
Child Ethnicity	Is this child Hispanic, Latino/a, or of Spanish origin? (Choose all that apply.)	No, not of Hispanic, Latino/a or Spanish origin; Yes, Mexican American, Chicano/a; Yes, Puerto Rican; Yes, Cuban; Yes, Another Hispanic, Latino/a or Spanish origin	HHS data standards (Dorsey & Graham, 2011)
Child Race	Which of the following best describes your child? (Choose all that apply.)	American Indian or Alaskan Native Asian; Black or African American; Native Hawaiian or Pacific Islander; White; Other (please describe)	U.S. Census, 2010
Parent Ethnicity	Are you Hispanic, Latino/a, or of Spanish origin? (Choose all that apply.)	No, not of Hispanic, Latino/a or Spanish origin; Yes, Mexican American, Chicano/a; Yes, Puerto Rican; Yes, Cuban; Yes, Another Hispanic, Latino/a or Spanish origin	HHS data standards (Dorsey & Graham, 2011)
Parent Race	Which of the following best describes you? (Choose all that apply.)	American Indian or Alaskan Native Asian; Black or African American; Native Hawaiian or Pacific Islander; White; Other (please describe)	U.S. Census, 2010
Parent Country of Birth	In what country were you born?	USA; Mexico; Somalia; Laos/Thailand/Vietnam; Other (please describe)	Adapted from (Marin & Gamba, 1996; Norris et al., 1996)
Child Country of Birth	In what country was this child born?	USA; Mexico; Somalia; Laos/Thailand/Vietnam; Other (please describe)	Adapted from (Marin & Gamba, 1996; Norris et al.,

Construct	Item	Response Options	Source
			1996)
Years Parent Lived in USA	How many years total have you lived in the United States?	_ _ yrs	Adapted from (Marin & Gamba, 1996; Norris et al., 1996)
Employment Status	What is your employment status?	Working full time; Working part time; Not working for pay	Developed
Marital Status	What is your current marital status?	Married or living as married; Single	Developed
Access to Car	Is there a car that you can use whenever you need to?	Yes and I drive; Yes but I don't drive; No	Developed
Frequency of Speaking English at Home with Family	How often do you speak English at home with your family? (Choose one.)	Never; Sometimes; About ½ the time; Most of the time; Always	Adapted from (Marin & Gamba, 1996; Norris et al., 1996)
	If you do not always speak in English at home with your family, what languages do you speak the rest of the time?	*Free text*	
WIC	Do you participate in WIC? WIC stands for Women, Infants, and Children, a Federal assistance program.	Yes; No; Don't know	Developed
Food Stamps/ SNAP	Does anyone in your household receive food stamps or SNAP? SNAP stands for Supplemental Nutrition Assistance Program.	Yes; No; Don't know	Developed
Unemployment/ Social Security/ Disability	Does anyone in your household receive Unemployment, Social Security, or Disability Benefits?	Yes; No; Don't know	Developed
Education Completed	What is the highest degree or level of school that you have completed? (Choose one answer.)	6th grade (elementary school) or less; 7th - 8th grade (attended some middle school/junior high); 9th - 12th grade (attended some high school); High school graduate (received diploma or the equivalent, GED for example); Completed some college credit, (or technical school) but no degree; Technical degree; Associate's degree; College degree; Master's, Professional, or Doctoral degree	Modified U.S. Census, 2010
	What is the highest degree or level of school that your child's	6th grade (elementary school) or less; 7th - 8th	Modified U.S. Census, 2010

Construct	Item	Response Options	Source
	other parent living in the household or adult caregiver living in the household has completed? (Choose one answer.)	grade (attended some middle school/junior high); 9th - 12th grade (attended some high school); High school graduate (received diploma or the equivalent, GED for example); Completed some college credit, (or technical school) but no degree; Technical degree; Associate's degree; College degree; Master's, Professional, or Doctoral degree	
Child Care	In a usual week, how much time does this child spend being cared for by someone other than parent/guardian…		Developed
	in your own home?	0 Hours; 1-10 Hours; 11-20 Hours; 21-30 Hours 31-40 Hours; 41+ Hours	
	in someone else's home?	0 Hours; 1-10 Hours; 11-20 Hours; 21-30 Hours 31-40 Hours; 41+ Hours	
	in childcare center/after school program?	0 Hours; 1-10 Hours; 11-20 Hours; 21-30 Hours 31-40 Hours; 41+ Hours	
Household Income	What was your total household income from all sources before taxes last year? By "household", we mean that you should report the combined income of everyone in your home.	$14,999 or less; $15,000 - $24,999; $25,000 - $34,999; $35,000 - $49,999; $50,000 - $74,999; $75,000 - $149,999; $150,000 - $199,999; $200,000 or more; Don't know; I prefer not to answer	Developed
Child Health Insurance	Is your child covered by a health insurance plan?	Yes; No; Don't know	
	Which type of plan are they covered by?	Medicaid, Medicare, CHIP, state funded, or other federally funded; Private - through work or purchased individually; Military; Other, type unknown; Don't know	
Free or Reduced Price Breakfast or Lunch	Does any child in your household receive free or reduced price breakfast or lunch at school?	Yes; No; Don't know	Modified from TAAG2

Construct	Item	Response Options	Source
Maturation Status	Has your daughter started having her menstrual period?	Yes; No; Don't know	Developed
	When did she have her first menstrual period?	MMYYYY	Developed
Breastfeeding/ Pregnancy Risk	Did <this child> breastfeed for more than a month?	Yes; No; Don't know	Schwarz et al. 2010
	How old was <this child> in months when he/she first received a bottle of formula, cow's milk, water, juice, tea, or cereal at least once a day?	_ _ mos.	Schwarz et al. 2010
	How much did this child weigh at birth?	_ _ lbs _ _oz	Schwarz et al. 2010
	Did a doctor say that <you/birth mother> had diabetes when pregnant with <this child>?	Yes; No; Don't know	Schwarz et al. 2010
	Did a doctor say that <you/birth mother> had hypertension (high blood pressure) when pregnant with <this child>?	Yes; No; Don't know	Schwarz et al. 2010
Food Security	"The food that (I/we) bought just didn't last, and (I/we) didn't have money to get more." Was that often, sometimes, or never true for (you/your household) in the last 12 months?	Often true; Sometimes true; Never true; Don't know; Refused	USDA (Bickel, 2000)
	"I/we couldn't afford to eat balanced meals." Was that often, sometimes, or never true for (you/your household) in the last 12 months?	Often true; Sometimes true; Never true; Don't know; Refused	USDA (Bickel, 2000)
	In the last 12 months, since (date 12 months ago) did (you/you or other adults in your household) ever cut the size of your meals or skip meals because there wasn't enough money for food?	Yes; No; Don't know; Refused	USDA (Bickel, 2000)
	How often did this happen -- almost every month, some months but not every month, or in only 1 or 2 months?	Almost every month; Some months but not every month; Only 1 or 2 months; Don't know; Refused; Not asked	USDA (Bickel, 2000)
	In the last 12 months, did you ever eat less than you felt you should because there wasn't enough money to buy food?	Yes; No; Don't know; Refused	USDA (Bickel, 2000)
	In the last 12 months, were you ever hungry but didn't eat	Yes; No; Don't know; Refused	USDA (Bickel, 2000)

Construct	Item	Response Options	Source
	because you couldn't afford enough food?.		
TV & Media	How many working TVs do you have in your home?	*text*	Derived from Borzekowski, 1999; Robinson, 1999; Robinson et al., 2010
	Is there a working TV in the room where <this child> sleeps?	Yes No	
	Is there a computer in your home?	Yes No	
	Is there a computer in the room where <this child> sleeps?	Yes No	
	Is there a video game player in your home?	Yes No	
	Is there a video game player in the room where <this child> sleeps?	Yes No	
	Do you have Internet access in your home?	Yes, No, Don't Know	
	On an average WEEK day, how many hours does <this child> watch TV?	None Less than 1 hour per day 1 hour per day 2 hours per day 3 hours per day 4 hours per day 5 or more hours per day	Schmitz et al., 2004
	On an average WEEKEND day, how many hours does <this child> watch TV?	None Less than 1 hour per day 1 hour per day 2 hours per day 3 hours per day 4 hours per day 5 or more hours per day	Schmitz et al., 2004
	On an average day, how many hours does <this child> play video or computer games, or use a computer for something that is not school work? (Include activities such as Play Station, Xbox, hand held video games, computer games, and the Internet.)	None Less than 1 hour per day 1 hour per day 2 hours per day 3 hours per day 4 hours per day 5 or more hours per day	Modified Schmitz et al., 2004
Food Norms	During the past seven days, how often did your family eat breakfast together?	0 times 1-2 times 3-4 times 5-6 times 7 or more times	Developed
	During the past seven days, how often did your family eat lunch together?	0 times 1-2 times 3-4 times	Developed

Construct	Item	Response Options	Source
		5-6 times 7 or more times	
	During the past seven days, how often did your family eat dinner together?	0 times 1-2 times 3-4 times 5-6 times 7 or more times	Developed
Weight Status	How would you classify your own weight?	Very Underweight Underweight Normal Overweight Very Overweight	Modified Birch et al., 2001
	How would you classify <this child's> current weight?	Very Underweight Underweight Normal Overweight Very Overweight	Modified Birch et al., 2001

9.1.2.2. Accelerometry

Background and Rationale
Physical activity (PA) will be measured objectively using a commercially available ActiGraph GT3X+ (all youth). For parents and other adults GT3X+ accelerometers (Vanderbilt) or GT3X accelerometers (Minnesota) will be used. (ActiGraph, Pensacola, FL). The rationale for using ActiGraph is that among currently available devices it provides consistent and high quality data supported by feasibility, reliability, and validity testing in children and adults.

ActiGraph monitors have been used in numerous studies to assess PA in children [127-130]. The validity of the ActiGraph has been examined in several studies involving children aged 2 to18 years. ActiGraph has been validated using direct observation [131-133], doubly labeled water (DLW) [134, 135], indirect calorimetry [136-140] and other accelerometers [132, 137] as reference methods. Correlations between ActiGraph counts and observed activity was moderate to high (r = 0.52-0.77) in older ActiGraph models [131-133] and higher in a newer ActiGraph (GT1M) model and when using more advanced algorithms [136]. Although the validity of ActiGraph GT3X and GT3X+ models in populations including children has not be reported, it is expected to be at least as high or higher than the GT1M and older ActiGraph models.

The GT3X+ and GT3X contain electronic motion sensors consisting of piezo-electric sensors that generate an electric charge in response to a mechanical force, thus, acceleration. They do not respond to constant acceleration. Their major advantage is that no power supply is required, except for data storage, resulting in a considerable reduction in the size and weight of the device. Both monitors provide activity counts, vector magnitude, and inclinometry data. Other data calculated by the ActiGraph manufacturer-provided software includes activity intensity levels, energy expenditure (METs) and number of steps.

The GT3X+ collects data in the raw format at a pre-defined sample rate from 30 to 100 Hertz (Hz). When collecting data at 40 Hz, the battery life is stated to be 13 days and the data memory lasts for 16 days. The GT3X has the ability to collect 1-second epoch data for at least 7 days. The GT3X does not have adequate data storage capacity to collect raw data for multiple days.

Accelerometry technology is still improving and mathematical models to predict PA and PA-related energy expenditure are being developed. We expect these advances to continue. Thus, COPTR investigators will collect raw acceleration data in the index child that could be used to measure physical activity and sedentary behavior using both currently existing algorithms and new algorithms/approaches that emerge during the study (next 6 years). Table 9.5 summarizes the specifications of the GT3X devices.

Table 9.5 Specifications of the GT3X devices

Specifications	**GT3X+**	**GT3X**
Transducer	Tri-axis, solid state accelerometer	Tri-axis, solid state accelerometer
Dynamic Range	+/- 3G	+/- 3G
Dimensions	4.6cm x 3.3cm x 1.5cm	3.8cm x 3.7cm x 1.8cm
Capacity	16 Days (Raw data at 40 Hz)	16MB or 400 Days (60 sec epoch)
Battery Life	13 Days (Fully Charged at 40 Hz)	20 Days (Fully Charged)
Weight	19 g	27 g
Resolution	12-bit A/D conversion; 1.46 mG (Raw Data)	12-bit A/D conversion; 1.46 mG (Raw Data)
Sample Rate	30Hz-100 Hz	30 Hz

Limitations of accelerometry.
Accelerometers are the best currently available relatively simple and precise device for objectively assessing physical activity and sedentariness. However, they do not provide information on types of activities, nor can they be used to assess lifestyle activities such as raking and shoveling, static activities such as bicycling and weight lifting, and aquatic activities such as showering and swimming. These limitations may be addressed as new algorithms emerge during the course of the study. Other limitations are related to use and application of collected data in device-specific arbitrary counts (PA counts) or more comparable approach of using acceleration (m/sec^2) to summarize accelerometry data.

Objective
Accelerometry monitoring will provide an objective measurement of the amount and patterns of physical activity and sedentary behavior.

Methods
Accelerometry data on children and parent (Minnesota and Vanderbilt) will be collected at four common data collection time points – baseline, 12 months, 24 months and 36 months. All baseline accelerometer data will be collected prior to randomization. The GT3X+ will be set to 40-Hertz frequency and the GT3X will be set to 1-second epoch.

The index children in the study will wear the GT3X+ monitor on the right hip for seven complete days (including while sleeping and naptime) except during water activity (e.g., bathing, swimming, showering). The responding parent in Minnesota and Vanderbilt will also wear the GT3X and GT3X+ monitor, respectively for seven days on their right hip. A consensus has been reached that the monitoring period should include two weekend days and five weekdays. In some cases, participants may be able to provide only 6 days of data, which is acceptable. If the participant does not wear the activity monitor for four days, it may be necessary to have the participant wear the monitor again in order to get valid data. The valid wear time criteria (minimums) are 4 days (3 weekdays and 1 weekend day) of at least 6 hours of awake time with 33% non-zero epochs per hour. For some participants, accelerometer data for the 2 wears will be combined in order to meet the minimum wear time criteria.

Any major updates in the ActiLife software version used during the trial will be made as a collaborative decision by the Diet and Physical Activity Working Group. If a change does occur, it will be on the same calendar day for all Field Sites. Regular (minor) updates in the ActiLife software will be done by each Field Site as they are released by ActiGraph. The Accelerometer Manual of Procedures will be updated only after major updates in the ActiLife software (e.g. Version 6.0 to Version 7.0).

COPTR will use a “train the trainer” model. Each field center will have at least two activity monitor master trainers who will participate in a central in-person training organized by the RCU at the University of North Carolina at Chapel Hill on April 16-18, 2012. Following part 1 of the training session, the master trainers will wear the accelerometer for at least 8 hours. The certification process requires the master trainer to successfully initialize, download and transfer accelerometer data. The master trainers will train and certify additional research staff at their site. Data collectors/staff do not initialize or download accelerometer data until after they have been trained and certified.

9.1.2.3. Dietary Assessment

Background and Rationale

The 24-hour recall is the most widely used method to assess diet in studies of populations, and is used in national food consumption surveys such as the NHANES. This method allows assessment of all foods, beverages and dietary supplements consumed during the 24-hour period obtained – typically beginning with the first item consumed the previous day. The 24-hour method, which can be performed face-to-face or by telephone, has been validated in lean and obese individuals (Conway, Ingwersen, & Moshfegh, 2004; Conway, Ingwersen, Vinyard, & Moshfegh, 2003). In face-to-face interviews, the use of visual aids such as food models, food portion booklets and measuring utensils improves the accuracy of estimation of quantities consumed (Moshfegh, Borrud, Perloff, & LaComb, 1999). For telephone interviews, visual aids and instructions are often mailed to subjects (Posner et al., 1992). In addition, with a trained interviewer, they are relatively quick and easy to administer. An important strength of the 24-hour recall method is that it allows comparison of groups of individuals by demographic variables such as age, gender, race/ethnicity or geographic region. Another strength is that the 24-hour recall (Nutrition Data Systems for Research or NDSR) has been used to generate Healthy Eating Index scores, and thus to assess dietary quality (Miller et al., 2011). The main limitations of capturing quantitative dietary intake information by use of 24-hour recalls are: 1) the variability in day-to-day dietary intakes; 2) reliance on subject memory; and 3) the potential of over or underreporting of intakes. To compensate for these possible limitations, interviewers typically capture data on more than one day of the week which includes both weekdays and weekend days, and use the USDA 5-step multi-pass method (Moshfegh, Borrud, Perloff, & LaComb, 1999).

Objective

The purpose of performing dietary intake assessment is to capture quantitative nutrient information on all the foods, beverages and dietary supplements that study subjects consume. The dietary intakes are analyzed for: volume of food, total energy, macronutrients, micronutrients, water, dietary fiber, added sugars and specific food groups. We will also examine glycemic load, dietary energy density, nutrient adequacy ratios, and dietary pattern and quality. Examples of diet quality indices used in children are shown in Table 9.6.

Table 9.6 Examples of dietary quality indices used in children

Citation	Subjects			Diet	Group/Index	Methods
	N	Sex	Age	Assessment		
Daniels, EJCN, 2009	1,810	m/f	2y	24 hr recall	Diet Diversity score(DDS-10g) - FAO (score 1-9)	Cross-sectional: 1 pt per 10g of a each food group or 1 pt for 1g oil.
Feskanich, JAmDietAssoc, 2004	16,452	m/f	9-14y	132 item FFQ	Youth HEI- 13 components (score 0-100)	Modified HEI and compared to YHEI (Note: YHEI not strongly related to energy intake).
Freedman, JNutr, 2010	17,311	m/f	≥2y	24hr recall	HEI-2005: 12 dietary components	NHANES ('01-'04) data- 3 part model (they create) based on Tooze 2- part model[141] in >1000 subjects.
Guenther, JAmDietAssoc, 2008	8,650	m/f	≥2y	24 hr recall	HEI-2005	NHANES ('01-'02) compared HEI-2005 assessed validity through 4 methods (concluded valid).
Kennedy, JNutr, 2007	3,164	m/f	24-71 mo	24 hr recall	Diet Diversity Score (DDS) – 10 food group & DDS-10g	Filipino Nutrition Database. DDS summed unique food groups for score. DDS-10g required minimum amounts (see: Daniels, 2009).
Manios, JAmDietAssoc, 2009	2,287	m/f	2-5y	24 hr recall + weighed records + food diaries	HEI- 10 component	Weighed records were used in nurseries and recalls or diaries were used outside nurseries. Summed individual scores- used quartiles of the scores for analysis.
Steyn, Public Health Nutr, 2006	2,200	m/f	1-8y	24 hr recall	DDS- following FAO guidelines Food Variety Score (FVS) (Score 0-45)	Secondary analysis of NFCS in South Africa. 1 24 hr recall by caregivers. Also used nutritional adequacy ratio and mean adequacy ratio.
Serra-Majem, EJCN, 2003	3,166	m/f	6-24y	24 recall +16 item FFQ	KIDMED- Mediterranean diet measure (Score: -3 to 12)	Assessed diet from Spanish children has high, med, low KIDMED.
Kranz, JAmDietAssoc, 2006	5,437	m/f	2-5y	24 recall	Created new- RC-DQI	Continuing Survey of Food intakes by individuals (1994-1996, 1998) components chosen based on My Food Pyramid, ADA, and APA recommendations (Nutrient-based)
Hurley, JNutr, 2009	317	m/f	11-19	131 item- youth/ adolescent FFQ	Compared HEI and YHEI	Compared the indices to body composition and found HEI better correlated with body composition and disease risk.
LaRowe, JAmDietAssoc, 2010	135	m/f	2-5	24 hr recall	My Food Pyramid	Great Lakes Inter-Tribal Council Head Start programs- baseline data from HCSF intervention.
Cheng, JNutr, 2010	376	m/f	6-8y	3-day weighed record	Nutritional Quality Index (NQI)- Density measure RC-DQI- nutrient based	German Cohort

Methods

Dietary Intakes will be measured using 24-hour recalls that are conducted on two weekdays and one weekend day per study time-point using NDS-R version 2012. Any update in the NDS-R version during the trial will be made as a collaborative decision by the Diet and Physical Activity Working Group. If a change does occur, it will be on the same calendar day for all Field Sites with one caveat. Participants who have already completed 1 or 2 recalls in the old version of NDS-R will have their remaining recalls conducted using the same older version of NDS-R such that all 3 recalls are collected using the same version of NDS-R.

Dietary assessment data will be collected at baseline, and 12, 24 and 36 months during the study. All baseline dietary assessment data will be collected prior to randomization. Table 9.11 summarizes the specific data collection plans for each Field Site. To avoid collecting days with similar foods, recalls should not be conducted on consecutive days. In addition, in order to capture variability of food supplies in the home, all three recalls should not occur within a seven day period. The third recall needs to be collected more than one week after the first recall. All three recalls must be collected within 30 days. This is a hard deadline. While the goal is to collect three dietary recalls per participant, it is possible that a limited number of participants at each Field Site may only have two dietary recalls completed within the 30 day window. All efforts will be made to obtain a minimum of two recalls (1 weekday and 1 weekend) for each participant. All dietary intakes (i.e., food, and beverages including water) will be collected. For Diet Recall of young children, those responsible for child feeding (e.g. parents, daycare providers) will be the reporter. Details of the procedures to be used in dietary assessment are in the COPTR Manual of Procedures for Dietary Assessment.

COPTR will use the "train- the- trainer" model. Each field center will have two diet master trainers who will participate in a central in-person training organized by the RCU at the University of North Carolina at Chapel Hill on April 16-18, 2012. Following the training session, the master trainers will complete two dietary recalls for certification by the RCU. The master trainers will train and certify additional research staff at their site. No diet recalls will be conducted until after the trainer has been trained and certified.

Table 9.7 Site specific 24 hour dietary recall data collection plans

	Case	Minnesota	Stanford	Vanderbilt
Number of recalls	3	3	3	3
# weekdays	2	2	2	2
# weekends	1	1	1	1
Recaller	Child & parent	Parent & day care provider	Child & parent	Parent & day care provider
How collected (1^{st}, 2^{nd}, 3^{rd})	In-person Telephone Telephone	In-person In-person/Telephone In-person/Telephone	In-person Telephone Telephone	Telephone Telephone Telephone
Announced/ Unannounced	Announced	Announced	Unannounced	Announced
Language administered	English	English, Spanish	English, Spanish	English, Spanish
Use of Portion Size Devices	Food Booklet	Food Booklet	Food Booklet	Food Booklet & Measuring Utensils

9.1.2.4. Blood Pressure

Background and Rationale

Elevated blood pressure (BP) in overweight children and adolescents is an increasingly recognized epidemic (Appel et al., 2006; Muntner, He, Cutler, Wildman, & Whelton, 2004; J. Sorof & Daniels, 2002; J. M. Sorof, Lai, Turner, Poffenbarger, & Portman, 2004). Many overweight/obese youth with elevated BP already have other cardiovascular risk factors and evidence of end-organ damage (Hanevold et al., 2004; National High Blood Pressure Education Program Working Group on High Blood Pressure in & Adolescents, 2004; Sinaiko, Steinberger, Moran, Prineas, & Jacobs, 2002; Sorof, 2002; J. M. Sorof, Alexandrov, Cardwell, & Portman, 2003; Sorof et al., 2004). Children with elevated BP are likely to become adults with elevated BP, and therefore are at increased risk for cardiovascular and renal disease (Appel et al., 2006; Bao, Threefoot, Srinivasan, & Berenson, 1995; Dekkers, Snieder, Van Den Oord, & Treiber, 2002; Gillman et al., 1993; Lewington et al., 2002). These data indicate that children with obesity and elevated BP are at particularly high risk, and require intervention (National High Blood Pressure Education Program Working Group on High Blood Pressure in & Adolescents, 2004). Weight loss is a powerful tool to reduce BP in children and adults (Appel et al., 2006; Rocchini et al., 1988). A diet rich in fruits/vegetables, low-fat dairy, low-fat protein (e.g. DASH-like diet) and/or reduced sodium intake can also reduce BP, particularly in African-American adults (Appel et al., 2006; Couch et al., 2008; Falkner, Sherif, Michel, & Kushner, 2000; He & MacGregor, 2006; Svetkey et al., 1999). Combined with calorie reduction, activity, and behavioral interventions, DASH diets facilitate simultaneous reduction of BMI and BP in adults (Elmer et al., 2006). However, the most effective methods to facilitate adoption of these lifestyle changes in children are not clear, and education alone (usual care) is often ineffective (Couch et al., 2008). This knowledge gap is particularly important because of the huge potential impact of small changes in BP (Appel et al., 2006). Therefore, blood pressure will be obtained for all participants from the two COPTR sites (Case Western Reserve University and Stanford University) testing interventions to treat overweight and obesity.

Objective

We will determine if interventions to reduce overweight and obesity reduce blood pressure. In addition we will use the 3-year longitudinal data to examine risk factors and correlates of blood pressure changes over time in children and adolescents.

Methods

An automated blood pressure measurement device (OMRON HEM-705-CP or OMRON HEM-705-CPN Digital Blood Pressure Monitor) and a standardized procedure for the measurement of blood pressure and pulse will be utilized, as specified in the Blood Pressure Manual of Procedures (MOP). The design and operation of the OMRON HEM-705-CP and the OMRON HEM-705-CPN Digital Blood Pressure Monitor are based upon the combined principles of compression of the brachial artery under an elastic, inflatable cuff and estimation of the systolic and diastolic blood pressure levels by oscillometric methods.

Blood pressure and pulse will be measured at four data collection time points – baseline, 12 months, 24 months and 36 months. All baseline blood pressure and pulse measurements will be collected prior to randomization. Blood pressure measurement must be conducted early in the visit and not following potentially stressful exam components such as the blood drawing. Before measurements commence participants are offered the opportunity to visit a restroom or bathroom. The participant should not have smoked or had any caffeine within the last 30 minutes prior to the blood pressure determinations.

Blood pressure measurements will be taken using the right arm. Participants should sit quietly for 4-5 minutes before the first measurement is taken. Seated, resting blood pressure and pulse are measured three times at each evaluation visit. The first reading will be discarded and the average of the second and third measurements will be used in analysis.

The OMRON HEM-705-CP and the OMRON HEM-705-CPN are automated devices. The data collector determines and places the correct size cuff on the participant's arm, pushes the button on the device and waits for the output. All readings will be recorded to the nearest integer.

COPTR uses a “train the trainer” model. Each Field Site designates two or more “master trainers” who participate in central trainings organized by the RCU at the University of North Carolina at Chapel Hill, NC from April 16 to April 18, 2012. The designated master trainers are responsible for training and certifying the data collection staff at their center. For certification, the data collector is observed by the trainer. The participants must include 5 or more children requiring varying cuff sizes. The trainee must correctly select the appropriate cuff size and demonstrate consistent compliance with the MOP to be certified. No blood pressure and pulse measurements will be taken until after the data collector has been trained and certified.

9.1.2.5. Biomedical Measures

Background and Rationale
Hyperinsulinemia/insulin resistance is a risk factor for future Type 2 diabetes, and is associated with increased blood pressure, adverse lipid profiles and increased body fatness in children and adolescents (Freedman, Dietz, Srinivasan, & Berenson, 1999; Garcia-Webb, Bonser, Wearne & Gracey, 1980; Gower, Nagy, Trowbridget, Dezenberg, & Goran, 1998), and weight loss is associated with improved insulin sensitivity among adolescents (Hoofman, Stumbo, Janz & Nielsen, 1995). Thus, insulin resistance serves both as a direct indicator of a significant risk factor and as a biochemical marker of metabolically-significant adiposity and changes in adiposity. Increased fasting insulin concentration is an appropriate marker of insulin resistance for this study.

Fasting insulin concentrations can also be combined with fasting glucose concentrations using a number of algorithms, including the HOMA and QUICKI, among others, to generate indices. However, all of these calculated measures of insulin resistance appear to be highly correlated with fasting insulin concentrations in non-diabetic subjects (Yeni-Komshian, Carantoni, Abbasi, & Reaven, 2000). The Stanford group have recently confirmed this with their own data from the 8-10 year old African-American girls in Stanford GEMS (correlations of .98-.99). However, because a fasting glucose will also be collected, the Field Sites will be able to examine each of these combination indices. Fasting glucose will also be collected to identify children with previously undiagnosed type 2 diabetes (fasting glucose ≥ 126 mg/dl) and to identify children who will be referred for further evaluation by their primary care medical provider (fasting glucose ≥ 110 mg/dl) according to Field Sites clinical monitoring protocol.

Adverse lipid profiles are risk factors for cardiovascular diseases and increased BMI is associated with increased total cholesterol, LDL-cholesterol, and triglycerides and lower HDL-cholesterol concentrations (J.T. Dwyer et al., 1998; Dwyer & Blizzard, 1996; Freedman et al., 1999; Laskarzewski et al., 1980; Zwiauer, Widhalm, & Kerbl, 1990). Thus, lipid measures also serve both as direct indicators of a significant risk factor and as a biochemical marker of metabolically-significant adiposity and changes in adiposity.

High levels of C-reactive protein (CRP) is a marker for inflammation. CRP prospectively assesses the risk of atherosclerotic complications, may be a mediator of vascular injury and is strongly related to obesity (Groner, Joshi, & Bauer, 2006). In adults, higher body mass index (BMI) levels are associated with higher CRP concentrations. Some clinicians are starting to use CRP levels when assessing risk for cardiovascular disease. Using cross-sectional data from the National Health and Nutrition Examination survey 1999-2000, Ford found significant associations between CRP levels and BMI in children 3 to 17 years of age (Ford, National, & Nutrition Examination, 2003). CRP levels were also associated with age and systolic blood pressure, but BMI had the strongest association.

Unexplained elevated levels of alanine Aminotransferase (ALT) has been liked with adiposity and may be a marker for nonalcoholic fatty liver disease (NAFLD) in adolescents and adults (Carrillo-Iregui et al., 2010; Park et al., 2005). Researchers have found a close association between metabolic syndrome, insulin resistance, elevated ALT levels and NAFLD in overweight/obese children and adolescents [142, 143]

Objective
We will determine if the COPTR interventions to reduce overweight and obesity change cardiovascular risk factors measured in blood. In addition we will use the 3-year longitudinal data to examine the risk factors and their correlates over time.

Methods
Blood specimens are collected at baseline, 12 months and 36 months at the two Field Sites testing interventions to treat overweight and obesity – Case Western Reserve University and Stanford University. All baseline blood specimen samples are collected prior to randomization. All blood specimens are analyzed by the Northwest Lipid Metabolism and Diabetes Research Laboratories (NWRL). The biomedical measures analyzed in the index child are Hemoglobin A1c (HbA1c), Glucose, Total Cholesterol, LDL-cholesterol, HDL-cholesterol, Triglycerides, high-sensitivity C-reactive protein (hs-CRP), Insulin and Alanine Aminotransferase (ALT).

Fasting status will be collected prior to blood draw. A trained phlebotomist at each site is responsible for the blood collection. However, a data collector might have the responsibility for mailing the blood specimens to the NWRL. All specimen samples will be frozen to allow for batch shipment. The assays and quality control for each measurement is described below.

HbA1c
The measurement of the relative proportion of hemoglobin subclasses and calculation of the HbA1c levels are performed by an NGSP-certified auto-analyzer (G-8 Tosoh, Biosciences, Inc.) using non-porous ion exchange high performance chromatography to achieve rapid and precise separation of stable HBa1c from other hemoglobin fractions. The system calibration is maintained using two point calibration reagents. A set of quality control samples are analyzed twice daily. The acceptance allowance for quality control is + 0.1% variance from the target value for the low level, and + 0.2% variance from the target value for the high level. The inter-assay CVs for the low and high quality control samples are 0.9% and 0.6%, respectively.

Glucose
Analysis of fasting and post glucose intake samples is performed enzymatically on a Roche Hitachi Modular P chemistry autoanalyzer. This instrument executes the glucose hexokinase method described by Schmidt (1961), Bergmeyer (1974) and Peterson and Young (1958) and recognized as the most specific method for the determination of glucose. Quality control

samples with normal and high glucose levels are used for monitoring glucose assay performance. The inter-assay CV is <3%. Lyophilized samples at two different glucose concentrations are used to monitor possible analytical drift.

Lipid Profile
Measurements of total plasma cholesterol in plasma, cholesterol in the lipoprotein fractions and triglycerides are performed enzymatically on the Roche Modular P autoanalyzer using methods standardized to the Centers for Disease Control and Prevention Reference Methods. Determination of HDL-cholesterol is performed after precipitation of apo B-containing particles by dextran sulfate Mg2+. LDL-cholesterol is calculated by the Friedewald equation. This approach for measuring LDL-CH is clinically reliable if the measurements of total CH, HDL-CH and triglycerides are performed with a high level of accuracy and precision. However, the Friedewald equation for the estimation of LDL-CH is inaccurate when triglycerides are >400 mg/dl. In this case, a complete lipoprotein separation by ultracentrifugation which allows quantitation of the individual lipoprotein classes is performed using the Lipid Research Clinics Beta Quantification procedure.

Quality control materials (BCL-Low, BCL-High (Biocell Laboratories) and L1-Medium (In-house prepared fresh frozen pool) are used at the beginning and at the end of each run.

The inter-assay CVs are consistently <1.5% for total cholesterol and triglycerides and <2% for HDL cholesterol.

Long-term Drift: A large quantity of two lyophilized quality control materials was acquired from Bio Rad for lipids. Values for each analyte were assigned by analyzing the samples daily for at least two weeks to achieve a minimum of 50 values. The mean of all the values constitutes the target value for each analyte. These materials are stored at -70°C and analyzed monthly to monitor for analysis drift. Actions are taken if the values are consistently above or below the 2 SD limit on two consecutive months.

C-Reactive Protein
Levels of C-reactive protein (CRP) in plasma are measured immunochemically on a nephelometer autoanalyzer (BNII). The reagents are obtained from Siemens Inc. This high sensitivity method is based on polystyrene particles coated with monoclonal antibodies specific to CRP which form immunocomplexes with CRP in plasma samples.The intensity of the scattered light in the nephelometer is directly proportional to the concentration of CRP which is determined versus dilutions of a standard of a known CRP concentration. The method is standardized against the IFCC/BCR/CAP reference preparation.

Insulin
The Insulin assay is a two site immuno-enzymometeric assay performed using Tosoh 2000 auto-analyzer. The assay is calibrated to WHO IRP 66/304 standard. The assay has a sensitivity level of 0.5 uU/mL and the standard curve linearity is up to 330 uU/mL. A set of high, medium and low insulin level controls are included in each batch of samples to monitor assay performance. The inter assay CVs for Low, Medium and High insulin level controls are 2.8%, 2.5% and 2.0% respectively. The assay has high specificity as cross- reactivity with Human C-peptide, intact Proinsulin, split (32, 33) Proinsulin and Des (64,65) proinsulin is 0%, 2 %, 2.6% and 39.8 % respectively. A Reference Interval for apparently healthy donors has been established at <17.0 uU/mL. The laboratory has participated in external proficiency evaluation program by the College of American Pathologists (CAP). Additionally, the laboratory has participated in the ADA sponsored Insulin Standardization workshops in 2007 and 2011. In the

2007 insulin standardization workshop this assay was reported as top performer with high sensitivity and specificity. Most recently, in 2011, ADA Insulin standard prepared and target level assigned by IDMS reference method was distributed to the laboratories. The ADA criteria of individual laboratory performance was set at up to 15.5% measurement bias from the assigned target level. Using the current insulin assay our laboratory achieved a bias less than 8.5%.

Alanine Aminotransferase (ALT)
This assay is performed on a Roche Double Modular P Analytics automated analyzer using Roche Diagnostics reagents. L-alanine reacts with alphaketoglutarate in the presence of ALT to form pyruvate and Lglutamate. NADH is then added to the pyruvate in the presence ofLDH to form L-lactate and NAD+. The rate of NADH oxidation to form NAD+ is directly proportional to the rate of pyruvate formation indicating ALT activity. The rate of decrease in absorbance at 340nm due to the formation of NAD is directly proportional to the rate of pyruvate formation and proportional to the ALT activity of the sample. The normal reference ranges for adults are: 17–67U/L (Male) and 13–50U/L (Female).

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9.1.3. Site-Specific Mediators, Moderators and Secondary Outcomes

Screen Time: Television Viewing, Computer use, Videotape/DVD Viewing and Video Game Use and other sedentary behaviors (secondary outcome, potential moderator, potential mediator): We will use the self-report instrument used in our studies of reducing screen time.[4, 36] These measures proved sensitive to change, a characteristic few, if any, other measures of children's media use have demonstrated. Children report the time they spent watching television, watching movies or videotapes on a VCR or DVD, playing on computers, and playing video games, separately for before school and after school, "yesterday" and "last Saturday." Prior to completion, children complete time-estimating exercises, to try to improve their time estimates. This instrument has demonstrated high test-retest reliability ($r = 0.94$)[22], and accuracy as compared to direct videotaped observation.[46] The instrument has also been revised to include newer types of media that can contribute to screen time (e.g., smart phones, iPads). The same instrument will be used for assessing other sedentary behaviors.

Eating Meals with the Television on (secondary outcome, potential moderator, potential mediator): Our intervention specifically targets eating while watching television. Children will report their past week's frequencies of eating breakfast, lunch, dinner and snacks in a room with the television turned on. These items were previously validated with direct videotaped observations,[46] and proved sensitive to change in our school-based television reduction study,[36] and in the Stanford GEMS Phase 1 Pilot Study.[4]

Household Television Use (secondary outcome, potential moderator, potential mediator). Parents/guardians report overall household television use with Medrich's constant TV households measure.[36, 144]

Sexual Maturation (potential moderator, potential mediator): Body fatness is related to children's sexual maturation stage.[145-148] We will measure sexual maturation stage as a potential moderator of treatment effects, by self-assessment using the Morris and Udry[149] drawings and descriptions of the five standard pubertal stages.[150] Prior studies have demonstrated that young boys and girls can accurately assess their sexual maturity,[149, 151-153] and self-assessments of sexual maturation in children show clinical validity.[148, 154-158] Self-assessment is more feasible and acceptable to participating children and their parents than a direct exam. Girls will also report their age at menarche, as a pubertal milestone that may help define early and later maturers.

Overconcern with Weight and Shape - McKnight Risk Factor Survey (MRFS) (secondary outcome, potential moderator, potential mediator): The Overconcern with Weight and Shape subscale of the MRFS[159] will be used to assess risk factors for eating disorders. As a secondary outcome, it is hypothesized that providing an effective weight gain prevention intervention may reduce girls' concerns about their weight and shape. As a potential moderator, girls who are more concerned about weight and overweight may respond differentially to treatment interventions compared to those with low levels of weight concerns. As a potential mediator, changes in concern about weight and overweight may influence weight change outcomes. The MRFS was developed and tested in multiple ethnicities, including Latina girls, by Drs. Taylor, Killen and Kraemer at Stanford and colleagues at University of Arizona.

Depressive Symptoms (secondary outcome, potential moderator, potential mediator): We use the 10-item short form of the Children's Depression Inventory (CDI), designed for use in children.[160]

School Performance (secondary outcome): School Performance is self-reported as "most recent school grades" on a 9-point scale ranging from "mostly A's (9) to mostly F's (1).[4] Because the intervention promotes reduced screen time and includes an after-school homework period we hypothesize that the intervention may result in improved school performance. Our expectations were substantiated by the nearly significant (P=.07) improvement in reported grades observed in the Stanford GEMS Pilot Study.[4]

Child Transportation to School (secondary outcome, potential moderator, potential mediator). Children report their mode of transportation to and from school in days per week.

Child Home TV/media environment (potential moderator, potential mediator). Parents/guardians are asked about the presence of TV's, cable or satellite, DVD or VCR players, DVRs, Portable DVD players, computers, internet access, wifi, video game players, digital music players, CD players, mobile phones, smart phones, tablet computers, to characterize the home media environment.

Child after-school physical activity programs and sports teams (potential moderator, potential mediator). At each annual data collection, parents/guardians are asked about their child's past participation in physical activity and sports with the questions: "Has your child participated in an after school physical activity program in the past year?" and "Has your child participated on a sports team in the past year?" [No, Yes, how many].

Child meals eaten outside the home and at school (potential moderator, potential mediator). Because our intervention involves changes to the home eating environment we are interested in meals eaten outside the home. At each annual data collection, parents/guardians are asked about their child's meals eaten outside the home. "In a typical week, how many days does your child eat breakfast outside the home?" [0-7] and "In a typical week, how many days does your child eat dinner outside the home?" [0-7] and "In a typical week, how many days does your child eat school lunches (lunches provided by school)?" [0-5].

Children's sleep habits (secondary outcome, potential moderator, potential mediator). Parents/guardians complete the abbreviated version of the Children's Sleep Habits Questionnaire (CSHQ) that has been previously validated in for preadolescents.

Child's unsupervised time (potential moderator, potential mediator) is assessed in parents/guardians for a typical weekday, Saturday and Sunday.

Family members' weight status (potential moderator, potential mediator). Parents/guardians report all household adult and children's weight status, very underweight to very overweight (5 levels), while reporting household membership.

Adult physical activity (secondary outcome, potential moderator, potential mediator). Parent/guardians report their frequency of exercising hard enough to breath hard and sweat, using questions developed and validated by Washburn, et al.[161, 162]

Implicit Theories (secondary outcome, potential moderator, potential mediator). In phase 1 we are developing measures of implicit theories of body weight, general habit formation, sports

ability and eating habits, for both children and parents, based on Dweck's studies of implicit theories of intelligence among adolescents.[106, 107] These questions distinguish between two different "theories" of body weight, habit formation, sports ability and eating habits as fixed (an "entity" theory) or malleable (an "incremental" theory). In the realm of academic performance, research has shown that, even when students on both ends of the continuum show equal intellectual ability, their theories of intelligence shape their responses to academic challenge.

Collection of Genetic material (potential moderator): The genetic basis of human obesity is considered to be particularly complex. Recent studies using genome-wide scans have revealed associations between common variants in genes such as FTO and MC4R with BMI, and more new loci associated with obesity are likely to be identified over time. In addition, the analytic technology is advancing at an extremely rapid rate. Therefore, we will collect biological material for DNA at baseline for use in analyses at the end of the study, when sequencing technologies will have substantially advance at reduced costs, and we have more information about specific candidate genes likely to contribute to human obesity and/or behavior change. Although power will be limited for genetic moderator analyses, we believe it is important to integrate genetic data into our models to be able to generate new multi-level hypotheses relevant to designing more effective interventions (and not just demonstrating observational associations). We are collecting both saliva samples and blood samples to produce sufficient samples and to be able to accommodate future preferences for sources of genetic material.

9.2. Quality Control

The overall goal of quality assurance is to assure complete, precise and accurate date. This is accomplished through monitoring the quality of the data collected and training and certification of the staff who collect the measurements. Biannually the RCU provides the DSMB Quality Assurance tables for the common measurements and site specific measurements.

9.2.1. Primary Outcome and Other Anthropometric Variables*

Ten percent (10%) of the measurements (height and weight) that compose the primary outcome (BMI) and the other anthropometric measurements (waist circumference and triceps skinfold) are measured by two different data collectors. Ideally one of the data collectors is a Master Trainer. The method used to select the 10% sample is site specific and is incorporated into the site's data management system to track who requires the second measurer. Duplicate measures are recorded to confirm inter-rater reliability, but the first data collection staff's measurements will be used in the analysis. To be acceptable, the absolute difference between the calculated values by the two data collectors must be less than 0.5 cm for height, 0.3 kg for body mass, 1 cm for waist, and no larger than 2 mm if the skinfold is less than 10 mm or greater than 10% if the skinfold is 10 mm or larger. If a data collection staff's agreement on a measurement (height, weight, waist circumference or skinfold) is outside this range in more than two out of ten individuals, then he/she must complete retraining.

Range checks are built into the data management system to prevent the collection of erroneous data. The 2003-2010 NHANES was used to determine age and gender-specific range checks for the anthropometric variables. Range checks are set so that participants with extreme and erroneous values are brought to the attention of the data collection staff for scrutiny.

The bounds for range checks in the baseline data collection vary by center since the anthropometric eligibility criteria for enrollment of index children vary.

9.2.2. Common Demographics, Mediators, Moderators and Secondary Outcomes*

The demographic variables are collected via questionnaires along with additional mediator variables (e.g. food security, tv and media). The survey collection, review and editing procedures are site specific. The RCU monitors for missing and out of range values on the common questions across the Field Sites.

Physical activity is measured by accelerometry. Because activity levels change daily and the test retest relationships would be low, participants are not asked to wear the activity monitor twice for quality control. In addition, an interview is not a good quality control check since it does not provide the necessary data for a comparison, and thus are not used for quality control. The RCU monitors and reports the amount of data (e.g. the number of valid days, number of re-wears). The valid wear time criteria (minimums) are 4 days (3 weekdays and 1 weekend day) of at least 6 hours of awake time with 33% non-zero epochs per hour. For some participants, accelerometer data for the 2 wears will be combined in order to meet the minimum wear time criteria.

The dietary interviewer reviews and edits the 24-hour dietary recall as soon as possible after its administration. During editing, special attention is paid to NDS-R Missing Foods, Priority Notes and all other Notes. Full quality assurance must be conducted on at least 10% of recalls. The quality assurance checks include ensuring information is entered correctly in header tab, meal information window, food tab and trailer tab. In the header tab the goal is to make sure information is filled in correctly (e.g. ID, Date of intake, Site ID). The meal information window should have meals in order by time and the eating and activity codes entered correctly. The quality assurance checks in the food tab include checking that foods entered correctly, amounts match code, missing foods and priority notes are resolved. Recalls that have issues that need to be resolved are put into the FIX project. All data must be cleaned and missing foods, or priority notes must be resolved before the output file is run and sent to the RCU on a quarterly basis. All missing foods are discussed at diet interviewer staff meetings. There will be quarterly reviews of data entry issues and shared user recipes to standardize the data entry process across all sites.

In SAS or other statistical package a quality assurance report is run to generate for each record total energy, percent kilocalories from fat, fruit servings, vegetable servings and grams of fluid. Ranges are set for school aged children and preschool aged children. Records with values beyond the cutoff points below are printed and checked.

	School Aged Samples	Preschool Samples
Total Energy	<500; >2500	<250; >1200
% kcal from fat	<25%; >45%	<25%; >45%
Fruit Servings	>3	>2
Vegetable Servings	>3	>2
Grams of Fluid	<300; >2000	<200; >1500

To protect against erroneous blood pressure and pulse measurements, computer entered data can be deleted and reentered as needed. Since the blood pressure and pulse measurement are collected using an automated device, end digit preference (e.g. 0 or 5) should not be an issue. Also, the OMRON blood pressure device does not require calibration. The RCU will calculate the correlations between the 2nd and 3rd blood pressure and pulse measurements within an individual.

All biomedical samples are sent to the Northwest Lipid Metabolism and Diabetes Research Laboratories, University of Washington (Seattle, WA, USA) for analysis. The laboratory participates in the Center for Disease Control and Prevention (CDC) lipids standardization program and is the Central Lab for several NIH sponsored studies. Standard procedures are implemented to ensure high quality data analysis and monitor for long term drift. See section 9.1.2.5. for specific quality assurance details for each lab measure.

9.2.3. Site-Specific Mediators, Moderators and Secondary Outcomes

- After the parent/guardian completes the surveys (paper & pencil), a data collection staff member carefully reviews each page of the survey. If a question has not been answered the data collector asks the question aloud to the parent/guardian before the visit is complete and mark the answer with a red pen directly on the paper survey. If more than one answer is marked, or it is unclear what answer the parent/guardian selected the data collector asks for clarification from the parent/guardian and use a red pen to circle the desired answer
- After a paper survey has been checked and corrected the data collector puts their initials on the front of the survey in the upper right hand corner where it says “DC initials”.
- Within one week of the visit the adult surveys are reviewed one more time by a data collector. If there are any missing or unclear items, the parent/guardian is contacted and the survey data is updated. Training by this data collector on common missed questions or likely problematic fields is provided to all data collection staff.
- The child survey is entered directly into FileMaker by the data collector conducting the interview; therefore, there is no need to manually check the answers to each question in the survey. Before the end of a data collection visit a data collector looks at the Child Summary section in FileMaker and be sure that all sections have a green highlighted “YES” indicating that the section is complete. A section that does not show “YES” is looked over again, and missing answers are re-asked of the child. Only when the “All Complete” box in the Child Summary appears as “YES” do the data collectors declare the visit complete and the record is locked against any inadvertent changes.
- After the visit all data collected in FileMaker is backed up by exporting a copy of the FileMaker entry onto the desktop. FileMaker contains a button that will perform this action automatically once clicked.
- Reports from the database are created and reviewed weekly by the Database Manager and Principal Investigator to ensure that visits are proceeding as expected.

9.3. Measurement Schedule

Data collection is scheduled for baseline, 12-, 24- and 36-months after the date of randomization. Assessment appointments will be scheduled to correspond as closely as possible to a ± 4-week window around the target date. However, because our primary outcome is the trajectory of BMI change, we can accommodate data collected at unequal intervals. Therefore, to maximize follow-up rates and minimize missing data, as a general rule we will continue to try to obtain follow-up data on participants who are beyond their target window for as long as six-months after the anniversary of randomization due date, or until it is clear that we will not be able to obtain their data. We will consider even longer time frames as well in unusual

circumstances where data are only available for during certain periods (e.g., a family that lives part of the year in Mexico).

10. PARTICIPANT SAFETY AND ADVERSE EVENTS MONITORING

10.1. Potential Risks and Protection against Risks

Potential risks are minimal and unlikely to occur. They include loss of confidentiality of self-report and measurement data, risk of injury during physical activity and assessments, and risk of temporary discomfort, bleeding and bruising from venipuncture, and of lightheadedness and fainting associated with venipuncture and blood pressure measurement. Overweight children and families seeking treatment are at increased risk of disordered eating.[82, 159, 163-167] Based on the nature of the experimental environmental interventions, it is unlikely they will increase that risk. Our past work suggests that providing healthful weight regulation strategies may reduce risk for disordered eating attitudes and behaviors among girls.[4, 164] The alternative to participation is to not participate.

We will recruit 240 families over approximately 18 months. 7-11 year old overweight and obese children and parents/guardians will be referred by their primary care provider or recruited through sites to participate in a weight control study comparing an enhanced standard care and health education program with the experimental multi-component, multi-level, multi-setting intervention. Study personnel will explain the study, complete a brief screening interview and schedule a baseline measurement appointment. Prior to baseline data collection, participation will be explained to children and parents/guardians in their preferred language (English or Spanish) along with potential risks and benefits and their rights to withdraw their consent at any time without prejudice, and signed consent will be required from parents/guardians for themselves and for their child, signed assent will be required from the children, and signed HIPAA authorization will be required from parents/guardians prior to participation. All recruitment and consent procedures will be approved by the Stanford University Administrative Panel on Human Subjects in Medical Research (IRB).

Based on the racial/ethnic composition of the local community and our experience in prior studies, we estimate the participants to be approximately 50% female, 58% Latino/Hispanic, 15% Black/African-American, 12% white, 10% Pacific Islander, 3% Asian, and 2% Native American/Alaska Native.

A data collection/tracking system will provide confidentiality to all participants. All collected data are identified by study identification numbers but not names. Only the study investigators will have access to lists linking study identification numbers and names. This list is stored separately from study data, in locked cabinets or password protected computers, in locked offices. Computer files containing data are password protected and stripped of identifiers as practicable. Consistent with Stanford University policy, all project staff will be required to complete the Human Subjects and HIPAA training modules for certification. These methods have proven successful at protecting confidentiality in our prior research.

Risks of injury during routine physical activity will be minimized by utilizing established protocols for warm-up and cool down. Team sports coaches will be trained by the investigators to conduct safe and enjoyable activity. Coaches will also complete the Human Subjects and HIPAA training modules and certification and Basic First Aid training prior to leading sports activities. It is conceivable that increased physical activity or contact with others, as a result of participation could lead to an increased number for injuries. Injuries and all adverse events (any medical illnesses or injuries requiring a visit to a medical care provider or institution) perceived to be related to participation will be assessed systematically in both treatment groups at each follow-up assessment. An adverse events recording form designed for this purpose systematically documents all adverse events occurring during the course of the study, whether or not they are thought to be related to participation (to at least include a brief description, severity, frequency, resolution, potential relationship to study participation, and action taken

with respect to study participation). Intervention staff will also be trained to investigate and record adverse events continuously, between assessments, as they become aware of them. The Stanford University Administrative Panel on Human Subjects in Medical Research (IRB), the DSMB and the NHLBI will be informed of all serious adverse events, and all adverse events, regardless of seriousness, will be reported during annual or semi-annual reports/reviews for the DSMB.

Overweight children and families seeking treatment are at increased risk of disordered eating.[82, 159, 163-167] Therefore, first, diagnosis of anorexia nervosa, bulimia nervosa or binge eating disorder, past or present, are exclusions for the study. Second, we screen all children and other household members for disordered eating using symptoms derived from the McKnight Risk Factor Survey (MRFS)[159] as part of the baseline assessments. If a child screens positive he/she is ineligible and we refer the family for psychological therapy. If an adult screens positive we require that they have prior approval and an ongoing relationship with a therapist before participating in the trial. Third, during treatment we will monitor weight changes. If a participant loses more than 5 Kg between annual measurement time points, we will specifically investigate whether he/she is skipping meals or severely restricting intake. Our interventionists and data collectors will also be trained to inquire about the use of unhealthy weight control methods throughout the treatment if they suspect unusual eating patterns or purging behaviors (including laxatives, diuretics, and OTC weight loss medications). All participants identified during treatment are referred for psychological evaluation and treatment and decisions about continuing the study are made with the input of their therapist. Finally, we also systematically assess weight concerns using the MRFS[159] in all participants as a secondary outcome measure at each annual measurement time point. In this way we will be able to identify whether the intervention as a whole unexpectedly puts participants at increased risk or, conversely (as we expect based on our past work[4, 164]) reduce their risk of unhealthful eating practices.

10.2. Potential Benefits

Participants may benefit from reduced weight gain and reduced physical, psychological and social morbidities and mortality associated with excess weight, the potential psychological and social benefits of participating in a community-based treatment program, the potential non-obesity-related health and behavioral benefits of reducing screen media use, and the potential health benefits of improved diet and activity behaviors. Other children and the public may benefit from the potential scientific and public health impact of the knowledge that may result from this study. The potential benefits to the subject and to others far outweigh the potential risks.

Importance of the Knowledge to be Gained. The United States is experiencing an epidemic of obesity in both children and adults. Childhood obesity is associated with substantial medical, psychological, and social morbidities.[1] For example, population-based data from Bogalusa, LA indicated that more than 60% of obese 5-10 year old children already suffered from at least one physiological risk factor for cardiovascular disease, such as hypertension, dyslipidemias, and/or hyperinsulinemia, and 25% had 2 or more risk factors.[168] Increased childhood obesity has also led to a new epidemic of Type 2 diabetes in children and adolescents, a problem that was previously limited to adults,[169-172] and now accounting for up to 45% of all newly diagnosed diabetes in children.[173] For children born in 2000, the lifetime risk of diabetes has been projected to be about 30 percent for boys and 40 percent for girls, and even higher among ethnic minority groups, at current obesity rates.[174] Autopsy studies of children who died from traumatic causes demonstrate that overweight children are already developing early atherosclerotic lesions in their aortas and coronary arteries.[175, 176] Conditions associated with overweight, such as sleep apnea and gallbladder disease, tripled in children and adolescents between 1979–1981 and 1997–1999.[177] Overweight children and adolescents also are much

more likely to become overweight adults.[178] And although overweight accounts for only 25 percent of adult obesity, overweight that begins before age eight and persists into adulthood is associated with a mean body-mass index of 41 in adulthood, as compared with a body-mass index of 35 for adult-onset obesity.[179] Long-term follow-up studies suggest that overweight children and adolescents may be at increased risk of total mortality[180] and mortality and morbidity from coronary heart disease, stroke, colorectal cancer, gout, and arthritis as much as 55 years later.[181] That estimated national direct and indirect health care costs from obesity range from about $98 billion to $129 billion (in 2004 dollars)[103] and account for about 9% of total U.S. medical spending.[182]. Therefore, there is a compelling rationale to try to prevent and reduce obesity in children, for its immediate and future benefits. Targeting efforts towards children may not only improve pediatric health, but potentially reduce and delay the incidence of chronic diseases in adults, such a heart disease, stroke, diabetes, and many cancers associated with obesity.

The history of obesity treatment has generally been one of relative disappointment. Many clinicians find obesity to be one of the most frustrating problems they deal with. Most treatments for children have produced only modest, unsustained effects,[77, 78] and some have been associated with health risks of their own.[79] Adult treatment results have generally been even more disappointing,[80] and minority adults appear to have less success than whites.[81] A systematic review of randomized, controlled trials of lifestyle interventions for the treatment of pediatric overweight concluded that most studies were too small and that the number of studies was insufficient to compare the efficacies of various treatment approaches or components.[2] In the absence of such data, studies of treatments in research settings,[77, 82] and of adult obesity,[83, 84] have provided the most useful direction.[1, 85]

We propose an innovative, interdisciplinary, multi-component, multi-level, multi-setting approach to treating overweight and obese children. We have designed this treatment model through a process of community based participatory research (CBPR) combined with past research findings, to overcome the major barriers to success from standard clinical and research treatment models. In addition, by utilizing existing resources in the community to provide an integrated treatment model, it is more generalizable to real world communities and populations. As a result, this research can be applied more broadly to improve children's health by reducing obesity-related morbidity and mortality.

10.3. Safety Monitoring Plan

The NHLBI has appointed a Data and Safety Monitoring Board (DSMB) to review study protocols and provide oversight of recruitment progress, data quality and completeness, efficacy monitoring, and participant safety. The DSMB will report to the NHLBI.

Monitoring Adverse Events: It is conceivable that an increase in physical activity could lead to an increased number of injuries. Injuries and all adverse events (any medical illnesses or injuries requiring a visit to a medical care provider or institution) perceived to be related to study participation will be assessed systematically in both treatment groups with an adverse events recording form as part of the annual follow-up assessments, by blinded data collectors. An adverse event is defined as both an expected side effect that is of serious nature or an unexpected side effect/event regardless of severity. We will, therefore, document all adverse events occurring during the course of the study (to include a brief description, severity, frequency, outcome, potential relationship to study participation, and action taken with respect to study participation). Intervention staff will also be trained to investigate and record adverse events continuously, between assessments, as they become aware of them. The DSMB and the Stanford University Administrative Panel on Human Subjects in Medical Research (IRB) will

be informed of all Serious Adverse Events, and all adverse events, regardless of seriousness, will be reported to the DSMB during annual or semi-annual reports/reviews.

Clinical Monitoring and Screening (additional procedures to promote participant safety): We will also screen participants for pre-existing or incident conditions that may pose a risk to their health, but are not expected to result from participation in the study. This represents an additional safety mechanism for study participants. Parents/guardians will be notified and referred to their primary medical care provider for further evaluation and care as needed, according to the parameters below. Notifications and referrals are made in writing, with a full explanation, and followed-up with subsequent phone calls to determine whether the child was medically evaluated.

• Growth: Adequate (normal) growth will be assessed from the baseline measure and subsequent serial measures of height, weight and body mass index, using current CDC national growth references (http://www.cdc.gov/growthcharts/). Children with a stature less than the 5th percentile for age will be notified and referred for further evaluation by their primary care medical provider. At follow-up visits, children growing at an average growth rate of less than 3.5 cm per year in stature, or crossing below the 5th percentile for age in height or BMI will be notified and referred for further evaluation by her primary care medical provider.

• Blood Pressure: Parents/Guardians of children with systolic or diastolic blood pressure >90th percentile for age, sex and height [183] will be notified and referred to their primary care medical provider. In addition, Stage 2 Hypertension, defined as more than 5mmHg above the 99th blood pressure percentile for age, gender and height percentiles will be an indication for prompt evaluation and treatment at the time of measurement. If the measured value indicates Stage 2 Hypertension, we will follow the procedure below.

1. Repeat the blood pressure measurement over again from the start.
2. If still greatly elevated (Stage 2 Hypertension) and...
    a. If symptoms: nausea, vomiting, headache, altered mental status, visual disturbance, seizure, neurological symptoms, or otherwise feeling ill, call 911 or immediate referral to the emergency room.
    b. If no symptoms (feeling perfectly normal): Refer to primary physician/clinic or Hypertension clinic within 48 hours. Tell them if they start to have any of the above symptoms or feel ill in any way, they must call 911 to go directly to the emergency room.

• Dyslipidemias: Parents/Guardians of children with a total cholesterol >200 mg/dl, LDL-cholesterol >130 mg/dl, HDL-cholesterol <35 mg/dl, triglyceride >135 mg/dl [184] will be notified and referred for further evaluation by their primary care medical provider.

• Fasting glucose: Parents/Guardians of children with impaired fasting glucose (>100 mg/dL) or diabetes (≥126 mg/dL) will be notified and referred for further evaluation by their primary care medical provider.

Screening for unhealthful eating behaviors. At baseline we screen all children, parents and other household members for a diagnosis of an eating disorder or disordered eating symptoms derived from the McKnight Risk Factor Survey (MRFS).[159] If a child screens positive he/he is ineligible and we refer the family for psychological therapy. If an adult screens positive we require that they have prior approval and an ongoing relationship with a therapist before participating in the trial. During treatment we will monitor weight changes. If a participant loses more than 5 Kg between annual measurement time points, we will specifically investigate whether he/she is skipping meals or severely restricting intake. Our interventionists and data collectors will also be trained to inquire about the use of unhealthy weight control methods throughout the treatment if they suspect unusual eating patterns or purging behaviors (including laxatives, diuretics, and OTC weight loss medications). All participants identified during

treatment are referred for psychological evaluation and treatment and decisions about continuing the study are made with the input of their therapist. Finally, we also systematically assess weight concerns using the MRFS[159] in all participants as a secondary outcome measure at each annual measurement time point. In this way we will be able to identify whether the intervention as a whole unexpectedly puts participants at increased risk or, conversely (as we expect based on our past work[4, 164]) reduce their risk of unhealthful eating practices.

Oversight of Participant Safety: The Principal Investigator has primary responsibility for the protecting the safety of study participants. The Principal Investigator, all Co-Investigators, and all study staff will complete the Stanford University training module in the Protection of Human Subjects prior to any contact with participants, and participant safety is accorded the highest priority in this study.

*Responsibilities of the Principal Investigator***:**

• Any change in the research protocol will be submitted to the IRB for review prior to the implementation of such change.

• Any complications in participants or evidence of increase in the original estimate of risk will be reported at once to the DSMB, the IRB and funding I/C before continuing with the project. The investigators will also inform the participants of any significant new knowledge obtained during the course of the research.

• All continuing projects and activities must be reviewed and re-approved at least annually by the IRB. IRB approval of any project is for a maximum period of one year. It is the responsibility of the investigator to re-submit the project to the IRB for annual review prior to the end of that year.

• All data including all signed consent form documents must be retained for a minimum of three years past the completion of the research.

• A summary of all adverse events will be reported to the DSMB for each meeting and will be reported annually to the IRB and the funding I/C as part of the annual renewal application.

• Any Serious Adverse Events (including deaths) will be reported to the DSMB and the funding I/C within one week of detection.

• The Principal Investigator will review study data on an annual basis for completeness and accuracy of the data as well as protocol compliance. A statement reflecting the results of the review will be sent to the funding I/C in the annual report (non-competing continuation).

Institutional (IRB) Responsibilities:

Institutional oversight will be provided by the Stanford University Administrative Panel on Human Subjects in Medical Research (IRB). Pursuant to HHS Regulations, it is the responsibility of the IRB:

(1) to determine if subjects are placed at risk, and if risk is involved, whether the risks to the subject are so outweighed by the sum of the benefit to the subject and the importance of the knowledge to be gained as to warrant a decision to allow the subject to accept these risks;

(2) to adequately protect the rights and welfare of any such subjects;

(3) to obtain legally effective informed consent by adequate and appropriate methods in accordance with HHS Regulations; and

(4) to review the conduct of the activity at timely intervals during the course of the project.

Data and Safety Monitoring Committee:

The NHLBI has appointed a Data and Safety Monitoring Board (DSMB) to review study protocols and provide oversight of recruitment progress, data quality and completeness, efficacy monitoring, and participant safety. The DSMB reports to the NHLBI. Confidentiality of participant data will be maintained throughout all DSMB reviews.

10.4. Informed Consent Documents

Following are our currently approved Consent, Assent and HIPAA authorization forms for the Pilot study and for Phase 2. We will revise Phase 2 forms in the next several months. Based on our experiences with multiple parents/adults associated with a participating child/children in the Pilot study, we intend to use separate forms for Parental Consent for Child Participation (one single form per child) and Parental/Adult Consent for their own participation (may be multiple forms associated with a single child).

CONSENT FORM

Clinic, Family & Community Collaboration to Treat Overweight and Obese Children
(Phase 1)

You are an adult subject in this study and/or
You are the parent or guardian granting consent for a minor in this study.

Print minor's name here: _____

Is your child participating in any other research studies? ____yes _____no

Are you participating in any other research studies? _____yes _____no

FOR QUESTIONS ABOUT THE STUDY, CONTACT: Drs. Thomas Robinson or Donna Matheson, Stanford Prevention Research Center, 1070 Arastradero Road, Suite 300, Palo Alto, CA 94304, phone: 650-723-5895.

DESCRIPTION: You and your child are invited to participate in a research study on the benefits of medical visits, community programs, and family strategies to help overweight children control their weight. Your family will participate in regular medical counseling about weight from your primary care provider or clinic and will be referred to participate in an after-school program at a local community center. Your family will be randomly assigned (like flipping a coin) to participate in one or more programs to help your child control his/her weight. These may include: (1) an after school sports program, (2) home visits to learn new skills to help your family change it's eating behaviors, (3) home visits to help your family control television and other screen media time and includes installing electronic television time managers, and/or (4) health and nutrition education newsletters and lectures.
You and your child also will be asked to complete study measurements before starting the program and at the end of the 3-month program. We will measure your child's height, weight, waist size, skinfold on the back of the arm, blood pressure and pulse rate, and we will ask how he/she spends his/her time, TV watching habits, what he/she eats, puberty, self-esteem, moods, and feelings about his/her weight. Your child will also wear a small activity monitor on a belt around his/her waist for up to 7 days, and we will call your child to ask about his/her eating twice more over the next several weeks. Before the start of the program only, we will also collect a fasting blood sample (about 11/2 tablespoons of blood) to test for cholesterol/lipid levels, glucose and insulin measures, and measures of inflammation and immunity, and ask your child to spit into a plastic tube to collect a small amount of saliva.

We will measure your height, weight, waist size, skinfold on the back of your arm, blood pressure and pulse rate, and you will be asked about your household food and eating habits. Once at the beginning of the study we will ask you about the make up of your and your child's family/household, annual income, education levels, race/ethnicity, and household TV viewing habits. We will also ask you and your child whether he/she has had any injuries or illnesses.
A total of about 40 families will participate in this study.
RISKS AND BENEFITS: The risks associated with this study are brief pain and bruising from blood tests and the possibility of increased injuries from increasing physical activity as part of this study. You and your child may benefit from this study with reduced weight and the improved medical, psychological and social benefits of losing weight, healthful eating, increased physical activity and less sedentary behavior. Other children, families, and the public may benefit from the scientific knowledge that results from this study. WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY BENEFITS FROM THIS STUDY. Your decision whether or not to participate in this study will not affect your or your child's medical care.

While participating in this research study, you should not take part in any other research project without approval from the Protocol Directors of each study. This is to protect you from possible injury arising from such things as extra blood drawing or similar hazards.
TIME INVOLVEMENT: Your participation in this experiment will last approximately 3 months. The two measurement visits, at the beginning and end of the study, are each expected to last about 1.5 to 2 hours. The after school program is available for your child in the afternoons after school and some weekends and holidays. If you are chosen for the home visits, these will last 1–2 hours and will occur up to six times over the three months. We will also ask you to visit your child's primary care medical provider or clinic to see your child once or twice for check-ins.
PAYMENTS: You will receive a $50 gift card per family for completing the beginning measures and a $50 gift card for the 3-month measures. All participants will receive membership to an after school program.

This study is sponsored by the National Institutes of Health.

You do not have to pay to participate in this study.

AUDIO, VIDEO AND PHOTOGRAPHIC RECORDING: Your and/or your child's voice and/or image may be recorded for later analysis. Some recordings may be shared with other researchers, or used at scientific meetings, to help them develop more effective weight control programs or describe the study. However, you will not be identified by name and your and/or your child's identity will be obscured where possible.

I give consent to be audiotaped during this study:

Please initial: ___Yes ___No

I give consent to be videotaped during this study:

Please initial: ___Yes ___No

I give consent to be photographed during this study:

Please initial: ___Yes ___No

Use of Blood and Saliva Samples for Future Research: In addition to using your child's blood and saliva for testing in this study, the researchers want to save your child's blood and saliva for future research. All the important scientific questions relating to this study may not be known at this time. New scientific information may be discovered that suggests additional questions requiring testing of blood and saliva from this study. There are several things you should know before allowing your child's blood and saliva to be stored for future research.
Your child's blood and saliva samples will be stored only with ID numbers and not with your child's name or other identifying information. The ID numbers will be unique to this study and not linked to your child's medical records. You will be informed of the results of the blood tests performed as part of this study but you will not be told the results of any future research tests.
As part of the future analysis on your child's blood and saliva samples, the investigators may do genetic research. Genetic research studies genes. Genetic research may include things like looking at whether the weight control program works better for children with some gene variations but not others. If your child's blood and saliva from this study is used for future genetic research, the results will be used for research purposes only, and you will not be told the results of the tests.

Genetic research raises certain questions about informing you of any results. Possible risks of knowing results include: anxiety; other psychological distress; and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

Any blood and saliva samples which are used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the Investigators, Stanford University and/or others. However, donors of tissues do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.
You have the right to refuse to allow your child's blood and saliva to be saved for future study.

_____ I consent to my child's blood and saliva samples being saved for future research

_____ I do not consent to my child's blood and saliva samples being saved for future research

PARTICIPANT'S RIGHTS: If you have read this form and have decided to participate in this project, please understand your and your child's participation is voluntary and you have the right to withdraw your and/or your child's consent or discontinue participation at any time without penalty or loss of benefits to which you and your child are otherwise entitled. You have the right to refuse to answer particular questions.

Your and your child's individual privacy will be maintained in all published and written data resulting from the study.

Data will be shared with other researchers and scientists not directly involved in the study. Other scientists may request data from this study but data will be released only after ensuring that your and your child's name and other identifying information are not given to any researcher or scientist.

Some of your child's blood test results and his/her progress and participation in the study will also be shared with the medical professional(s) or clinic that you identify as your child's primary care provider and/or clinic.

CONTACT INFORMATION:
Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Dr. Thomas Robinson (650-723-5895). You should also contact him at any time if you feel you have been hurt by being a part of this study.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or

your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, Stanford, CA 94305-5401.

EXPERIMENTAL SUBJECTS BILL OF RIGHTS:

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

The extra copy of this consent form is for you to keep.

_____ _____

Signature of Legally Authorized Representative (Parent or Guardian) Date

_____

Printed Name

_____

Description of Representative's Authority to Act for Minor Subject

_____ _____
(If available) Signature of Other Parent or Guardian Date

_____
Printed Name

_____
Authority to act for participant

The IRB determined that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404, in accordance with 45 CFR 46.408(b)

Person Obtaining Consent

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied – that the subject has been provided with the Experimental Subject's Bill of Rights, if appropriate, that I have discussed the research project with the subject and explained to him or her in non-technical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the subject to ask questions and that all questions asked were answered.

_____ _____
Signature of Person Obtaining Consent Date

ASSENT FOR CHILDREN

Clinic, Family & Community Collaboration to Treat Overweight and Obese Children
(Phase 1)

You are invited to join a Stanford medical study to help overweight children.

Your parent or guardian has been told about this study and has agreed for you to join. You only have to join this study if you want to.

If you join the study or don't join the study you will not be treated any differently by Stanford. Once you join the study you may change your mind and stop later.

If you join the study it will last for about 3 months. At the beginning you will visit us with your parent or guardian to have your height, weight, waist, the skin on the back of your arm, blood pressure, pulse measured, and to collect saliva and blood. We will ask you questions about things like your health, how much you play and watch TV, and how you feel. You will also be asked to wear a little gadget on a belt around your waist for about 7 days in a row to measure how much you move and you will be asked to tell us everything you eat in a day on three different days. We will telephone you to get this information. Blood and saliva will only be collected at the beginning of the study but the other measures will all be repeated at the end of the study.

During the three months you will be able to attend an after school program. If you are chosen (like flipping a coin) you will also be able to participate in other programs. This may include attending an after school sports program, having a Stanford researcher visit you at home up to 6 times to teach your family how to help your eating and/or to give you ways to spend less time watching TV and movies, playing on the computer, or with computer games, and/or receiving nutrition and health newsletters in the mail and attending health classes.

This study is not dangerous.

Joining this study may be fun and you may improve your eating and your health habits. But we do not promise that this study will be good for you.

Only the scientists at Stanford, some scientists at other places, and your doctor, nurse or clinic will see the information we collect from you. We will not show it to your school or anyone else.

We may also take sound recordings, videos, and pictures of you that we may show to other people who are in the study or who might be interested in joining the study, and/or show them to other scientists to help them.

Your family will be paid a $50 gift card after the measures at the beginning of the study and another $50 gift card after the measures at the end of the study.

You and your family will not have to pay to be in this study.

If you have any questions about joining the study we want you to ask us. If you think of more questions later, you can ask your parent or guardian to call us to get the answer, or you can call us at (650) 723-5895.

If you have any problems with this study tell your parent or guardian.

If you are not happy about this study or if you have any questions, please contact the Stanford Institutional Review Board (IRB) to speak to someone other than your doctor at (650)-723-5244 or toll free at 1-866-680-2906 or write the Stanford IRB, Administrative Panels Office, Stanford University, Stanford, CA 94305-5401.

Do you understand this study and are you willing to participate?

YES ____ NO ____

_____ _____

Signature of Child Date

CONSENT FORM

Clinic, Family & Community Collaboration to Treat Overweight and Obese Children
(Phase 2)

You are an adult subject in this study and/or
You are the parent or guardian granting consent for a minor in this study.

Print minor's name here: _____

Is your child participating in any other research studies? ____yes _____no

Are you participating in any other research studies? _____yes _____no

FOR QUESTIONS ABOUT THE STUDY, CONTACT: Drs. Thomas Robinson or Donna Matheson, Stanford Prevention Research Center, 1070 Arastradero Road, Suite 300, Palo Alto, CA 94304, phone: 650-723-5895.

DESCRIPTION: You and your child are invited to participate in a research study on the benefits of medical clinic, community, and family strategies to help overweight children control their weight. Your family will participate in regular medical counseling about weight from your primary care provider or clinic and will be referred to participate in an after-school program at a local community center. In addition, your family may be randomly chosen (like flipping a coin) to participate in a different after school sports program and to receive home visits to give you new glasses, plates, bowls, and other kitchenware to help prevent overeating and to learn new strategies to reduce television watching. You and your child will be asked to complete study measurements before starting the program and at the end of the 12-, 24- and 36-months, at the end of the program.

We will measure your child's height, weight, waist size, skinfold on the back of the arm, blood pressure and pulse rate, and we will ask how he/she spends his/her time, TV watching habits, what he/she eats, puberty, self-esteem, moods, and feelings about his/her weight. We will also collect a fasting blood sample (about 2 teaspoons of blood) to test for cholesterol/lipid levels, glucose and insulin, and inflammation. Your child will also wear a small activity monitor on a belt around his/her waist for up to 7 days, and we will call your child to ask about his/her eating twice more over the next several weeks.

We will measure your height, weight, waist size, skinfold on the back of your arm, blood pressure and pulse rate, and you will be asked about your household food and eating habits. Once at the beginning of the study we will ask you about the make up of your and your child's family/household, annual income, education levels, race/ethnicity, and household TV viewing habits. We will also ask you and your child whether he/she has had any injuries or illnesses.

A total of about 240 families will participate in this study.

RISKS AND BENEFITS: The risks associated with this study are brief pain and bruising from blood tests and the possibility of increased injuries from increasing physical activity as part of this study. You and your child may benefit from this study with reduced weight and the improved medical, psychological and social benefits of losing weight, healthful eating, increased physical activity and less sedentary behavior. Other children, families, and the public may benefit from the scientific knowledge that results from this study. WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY BENEFITS FROM THIS STUDY. Your decision whether or not to participate in this study will not affect your or your child's medical care.

While participating in this research study, you should not take part in any other research project without approval from the Protocol Directors of each study. This is to protect you from possible injury arising from such things as extra blood drawing or similar hazards.

TIME INVOLVEMENT: Your participation in this experiment will last approximately 36 months. The four measurement visits, at the beginning and every year, are each expected to last about 1 to 1.5 hours. The after school program is available for your child in the afternoons after school and some weekends and holidays. If you are chosen for the home visits, these will last 1 – 2 hours and will occur about 8 times over three years. We will also ask your child's primary care medical provider or clinic to see your child about every 3-6 months for check-ins.

PAYMENTS: You will receive $50 per family for completing the beginning measures, $50 per family for completing the 12-month measures, $50 per family for completing the 24 month measures, and $100 per family for completing the final 36 months measures. Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa.

This study is sponsored by the National Institutes of Health.

You do not have to pay to participate in this study.

AUDIO, VIDEO AND PHOTOGRAPHIC RECORDING: Your and/or your child's voice and/or image may be recorded for later analysis. Some recordings may be shared with other researchers, or used at scientific meetings, to help them develop more effective weight control programs or describe the study. However, you will not be identified by name and your and/or your child's identity will be obscured where possible.

I give consent to be audiotaped during this study:

Please initial: ___Yes ___No

I give consent to be videotaped during this study:

Please initial: ___Yes ___No

I give consent to be photographed during this study:

Please initial: ___Yes ___No

Use of Blood Samples for Future Research: In addition to using your child's blood for testing in this study, the researchers want to save your child's blood for future research. All the important scientific questions relating to this study may not be known at this time. New scientific information may be discovered that suggests additional questions requiring testing of blood from this study. There are several things you should know before allowing your child's blood to be stored for future research. Your child's blood samples will be stored only with ID numbers and not with your child's name or other identifying information. The ID numbers will be unique to this study and not linked to your child's medical records. You will be informed of the results of the blood tests performed as part of this study but you will not be told the results of any future research tests.

Tissue Sampling for Genetic Testing

As part of the analysis on your child's samples, the investigators may do genetic testing. Genetic research is research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment. Genetic research raises certain questions about informing you of any results. Possible risks of knowing results include: anxiety; other psychological

distress; and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.
If your child's blood from this study is used for future genetic research, the results will be used for research purposes only, and you will not be told the results of the tests.

Any blood samples which are used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned by the Investigators, Stanford University and/or others. However, donors of tissues do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.
You have the right to refuse to allow your child's blood to be saved for future study.

_____ I consent to my child's blood samples being saved for future research

_____ I do not consent to my child's blood samples being saved for future research

PARTICIPANT'S RIGHTS: If you have read this form and have decided to participate in this project, please understand your and your child's participation is voluntary and you have the right to withdraw your and/or your child's consent or discontinue participation at any time without penalty or loss of benefits to which you and your child are otherwise entitled. You have the right to refuse to answer particular questions.

Your and your child's individual privacy will be maintained in all published and written data resulting from the study.

Data will be shared with other researchers and scientists not directly involved in the study. Other scientists may request data from this study but data will be released only after ensuring that your and your child's name and other identifying information are not given to any researcher or scientist.

To help us protect your and your child's privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you or your child, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, except as explained below. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. The researchers will use the Certificate to resist any demands for information that would identify you or your child, except for voluntary disclosures about things such as child abuse, intent to hurt self or others, or other voluntary disclosures. The Certificate of does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you and your child as participants in the research project if judged to present a danger to you, your child or others.

CONTACT INFORMATION:
Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Dr. Thomas Robinson (650-723-5895). You should also contact him at any time if you feel you have been hurt by being a part of this study.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, Stanford, CA 94305-5401.

EXPERIMENTAL SUBJECTS BILL OF RIGHTS:
As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;

- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

The extra copy of this consent form is for you to keep.

_____ _____
Signature of Legally Authorized Representative Date
(Parent or Guardian)

_____
Printed Name

_____
Description of Representative's Authority to Act for Minor Subject

_____ _____
(If available) Signature of Other Parent or Guardian Date

_____
Printed Name

_____
Authority to act for participant

The IRB determined that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404, in accordance with 45 CFR 46.408(b)

Person Obtaining Consent

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied – that the subject has been provided with the Experimental Subject's Bill of Rights, if appropriate, that I have discussed the research project with the subject and explained to him or her in non-technical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the subject to ask questions and that all questions asked were answered.

_____ _____

Signature of Person Obtaining Consent Date

ASSENT FOR CHILDREN

Clinic, Family & Community Collaboration to Treat Overweight and Obese Children
(Phase 2)

You are invited to join a Stanford medical study to design ways to help overweight children

Your parent or guardian has been told about this study and has agreed for you to join. You only have to join this study if you want to.

If you join the study or don't join the study you will not be treated any differently by Stanford. Once you join the study you may change your mind and stop later.

If you join the study it will last for 3 years. At the beginning you will visit us with your parent or guardian to have your height, weight, waist, the skin on the back of your arm, blood pressure, pulse and a blood test taken. We will ask you questions about things like your health, how much you play and watch TV, and how you feel. You will also be asked to wear a little gadget on a belt around your waist for about 7 days in a row to measure how much you move and you will be asked to tell us everything you eat in a day on three different days. We will telephone you to get this information. These measures will all be repeated every year until the end of the study (3 more times).

During the three years you will be able to attend an after school program. If you are chosen (like flipping a coin) you will attend a different after school program and a Stanford researcher will also visit you at home up to 8 times to bring your family new dishes to help your eating and to give you ways to spend less time watching TV and movies and playing on the computer or with computer games.

This study is not dangerous.

Joining this study may be fun and you may improve your eating and your health habits and gain less weight. But we do not promise that this study will be good for you.

Only the scientists at Stanford and some scientists at other places will see the information we collect from you. We will not show it to your school or anyone else and we will not use your name.

We may also take videos and pictures of you that we may show to other people who are in the study or who might be interested in joining the study, and/or show them to other scientists to help them.

Your family will be paid $50 after the measures at the beginning of the study, another $50 after the measures after 1 and 2 years, and $100 after the measures after 3 years.

You and your family will not have to pay to be in this study.

If you have any questions about joining the study we want you to ask us. If you think of more questions later, you can ask your parent or guardian to call us to get the answer, or you can call us at (650) 723-5895.

If you have any problems with this study tell your parent or guardian.

If you are not happy about this study or if you have any questions, please contact the Stanford Institutional Review Board (IRB) to speak to someone other than your doctor at (650)-723-5244 or toll free at 1-866-680-2906 or write the Stanford IRB, Administrative Panels Office, Stanford University, Stanford, CA 94305-5401.

Do you understand this study and are you willing to participate?
YES ____ NO ____

_____ _____
Signature of Child Date

IRB Meeting date: 7/15/11

Authorization To Use Your Health Information For Research Purposes

Because information about you and your child, and your and your child's health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your and your child's health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

Your and your child's health information will be collected during this study to evaluate the benefits of linking primary care medical providers with community after school programs and family strategies to help overweight and obese children control their weight. All information collected during this research -- including surveys and interviews, laboratory measures, and physical measures -- will be kept confidential and results will not be disclosed to anyone without your permission except as described below. Information may be released to the National Heart, Lung, and Blood Institute of the National Institutes of Health (the sponsor of the research) and to other researchers for scientific purposes, but only after removing your and your child's name and all other personal identifiers. Any data published or presented at scientific meetings will not reveal the identity of the participants.

Do I have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you and your child will not be able to participate in this research study, including

receiving the research-related treatment. Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?

If you and your child decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your and your child's health information (and to discontinue any other participation in the study) at any time. After any revocation, your and your child's health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your and your child's information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your and your child's health information in this study, you must write to: Dr. Thomas Robinson, Stanford Prevention Research Center, 1070 Arastradero Road, Suite 300, Palo Alto, CA 94304.

What Personal Information Will Be Used or Disclosed?

Your and your child's health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to, names, phone numbers, addresses, email addresses, and birth dates, in addition to your and your child's answers to surveys and interview questions, physical measurements, and blood tests collected specifically for this study.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director, Dr. Thomas Robinson.
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary.
- Other Stanford researchers working on this study.
- Research Staff working on this study.

Who May Receive or Use the Information?

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The medical professional(s) or clinic that you identify as your child's primary care provider and/or clinic
- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- The National Heart, Lung, and Blood Institute of the National Institutes of Health.
- The Data & Safety Monitoring Board of scientists who review the study for safety and integrity.
- Scientific collaborators outside of Stanford who are working on this study.
- Other researchers for scientific purposes, but only after removing your and your child's name and all other personal identifiers.

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?

Your authorization for the use and/or disclosure of your health information will expire on December 31, 2099.

Will access to my study information be limited during the study?

To maintain the integrity of this research study, you may not have access to any information developed as part of this study, except the results we report to you. The information we collect as part of this study will not be included in your or your child's official medical record at Stanford University Hospital or Lucile Packard Children's Hospital.

_____ _____

Signature of Legally Authorized Representative (Parent or Guardian) Date

_____
Description of Representative's Authority to Act for Minor Subject

_____ _____
(If available) Signature of Other Parent or Guardian Date

_____
Authority to act for participant

The IRB determined that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404, in accordance with 45 CFR 46.408(b)

11. STUDY DESIGN, STATISTICAL CONSIDERATION AND ANALYSIS PLAN

11.1. Study Design

Two-arm, parallel group, randomized controlled trial.

11.2. Primary Research Question and Hypothesis

Will a 3-year, innovative, interdisciplinary, multi-component, multi-level, multi-setting (MMM) community-based intervention to treat overweight and obese children significantly reduce BMI compared to a standard care/health education active placebo control intervention?

Primary Hypothesis: Compared to standard care/health education controls, children randomized to our multi-component, multi-level, multi-setting (MMM) intervention will have a significantly attenuated body mass index trajectory.

11.3. Primary Outcome

The primary objective of the proposed intervention is to reduce BMI to a degree that has clinical and/or public health and policy significance. We will assess our success by comparing changes in the treatment and control groups over the course of the entire 36-month study. To do so, we propose an analytic strategy that takes full advantage of the prospective nature of the data collected. For the reasons described above, rate of change in body mass index has been chosen as the primary outcome measure. To that end, BMI will be assessed at baseline, and at approximately 12-, 24- and 36-months after baseline. Our primary outcome is a derived measure of change in BMI values for each child. More specifically, change in BMI will be estimated by computing a slope for each child by regressing BMI on time, where each child may have up to 4 BMI measurements (at baseline, 12 months, 24 months, and 36 months post randomization), and by assuming that BMI behaves linearly over time. Children with at least 2 measurements will have a corresponding derived slope. Children with only one BMI measurement at baseline, however, will have missing outcome values (slopes), which will be imputed via multiple imputation techniques as described below. One important, practical advantage of this approach is that it incorporates BMI measurements obtained at varying intervals. While we intend to assess follow-up BMI at 12, 24 and 36 months after baseline, experience suggests this does not always occur. In contrast to other possible functional forms of the outcome, the proposed approach allows and accounts for deviation from the ideal measurement schedule without unrealistic assumptions about timing that may introduce substantial additional error into the outcome.

11.4. Primary Analysis

11.4.1. Statistical model and approach:

As the derived outcome (slope representing rate of change in BMI) removes the correlation of observations within a subject, regression methods that assume independence across observations will be employed. More specifically, ANCOVA is the method that will be applied for the primary analysis. The proposed model can be expressed as:

BMI Slope = beta0 + beta1 treatment + beta2 baseline BMI (centered by average BMI) + beta3 baseline BMI (centered by average BMI) x treatment + epsilon,

where epsilon is the random error term assumed to follow a normal distribution.

We will use multiple imputation (MI) techniques to multiply impute outcomes (slopes) for children without slope measurements (those children with only a baseline measurement) using the fully conditional specification approach of imputation. MI allows inclusion of all children randomized to treatment arm so we can perform an intent-to-treat analysis (described below).

To address the primary aim, we will test the hypothesis corresponding to overall treatment effect. All tests will be two-sided and conducted at the 0.05 level of significance.

Why include the Treatment x baseline BMI interaction as a covariate? Often, Treatment x baseline feature interactions are used only in secondary analyses, to assess whether the intervention is more or less effective among different groups of participants. While that is also of interest to us, that is not why we include the interaction term in our primary analysis of treatment effects. In earlier studies we have occasionally found evidence of greater effects of behavioral interventions among participants with greater or lesser BMI at baseline.[4, 8, 36] We therefore include the Treatment x baseline BMI interaction effect as a term in the model to obtain an unbiased estimate of treatment effects. Although this is not often seen in the reports of clinical trials, it has been well acknowledged and recommended for decades in the statistical literature.[185-188] To ignore a strong interaction in the model has three effects: (1) Part of the interaction effect (in non-orthogonal designs) is remapped into the main effects, thus producing a biased estimate of the main effect of treatment; (2) Part of the interaction effect (whether or not the design is orthogonal) is remapped into the error sum of squares, with consequent possibly substantial reduction of power; and (3) Since the residual variance used in estimating effect sizes is inflated, it is quite possible that the effect size of treatment will be attenuated, thus misleading consideration of the clinical significance of the treatment. If our expectation is wrong, and there is no non-zero Treatment x baseline interaction, then this analysis still results in an unbiased estimate of the main effect of Treatment, and we only lose one degree of freedom. Thus the effects of ignoring a strong interaction generally far outweigh the risks of including an unnecessary interaction. As a result, including a Treatment x baseline BMI term in the primary analysis is the best strategy for this study. It insures that we will have an unbiased estimate of the main effect of treatment and potentially increases our power.

11.4.2. Assumptions with Justification

Assumption of Linear Trajectories of BMI: To help determine whether a linearity assumption is appropriate for BMI changes for the Stanford COPTR trial we examined BMI data from four prior RCTs or longitudinal studies performed at Stanford. We limited these analyses to the participants in these studies that would most closely represent our proposed study sample in terms of age, baseline BMI (≥ 85th percentile for age), and ethnicity. Our investigation involved three different approaches and the results can be summarized as follows:

1) We evaluated graphical trends of observed BMI over time for each treatment arm (for those studies with multiple treatment arms), for each age group at entry, and for gender. Graphical evidence for linearity was strong. We plotted the average observed BMI at a given time point for each group over time and they largely demonstrate a linear trend over the

study periods. These results also are consistent with the published trajectories of BMI in this age group illustrated in the extant literature identified by the RCU.

2) We assessed coefficients from more flexible, mixed effects regression models that allow BMI change to be non-linear over time. The coefficients corresponded well to the plots and demonstrated monotonic increases in BMI over time and, in general, largely linear trends.

3) We conducted formal tests comparing a model assuming linear changes in BMI over time versus one that assumes a quadratic relationship between BMI and time (including both a linear and squared term). The test of the null hypothesis was performed for each relevant subgroup (18 tests across the four studies) and the null hypothesis was rejected in only one case (ECHALE study, age 8, control group).

Therefore, the findings from all three approaches support the assumption that BMI changes are likely to be linear over the Stanford COPTR age range. Our findings are also consistent with the trajectories shown in the published literature and are expected when fitting four annual time points. In addition, our intention to implement our intervention over the entire 3-year study period is also consistent with the assumption of linear BMI changes. Based on these results, we believe an assumption of linear changes in BMI over the study period, with annual measures for both treatment and control arms, is most appropriate.

Assumption of independence of observations across participants: An analysis plan should be selected to most closely mirror the study design. In this study, participants are randomized at the individual household level and only one randomly chosen eligible child from each family/household is included in the analysis, eliminating the possibility of clustered responses within families/households. In studies where children receive their intervention in groups or at specific sites, consideration must be made (e.g., through models that allow incorporation of random effects or by making use of robust standard error estimates) of clustering by groups/sites that induces a correlation among responses from participants at given groups/sites. Not doing so can result in underestimated standard error estimates and consequently inflated Type I error rates.

In our study, however, our design induces no such natural clustering and, furthermore, any potential clustering will be very difficult to define. Partly this is because the intervention is multi-faceted and largely administered on an individual level in multiple settings, at community centers, in primary care medical settings, and at participants' homes. Each participating child will therefore not experience the intervention with any consistent group of other children over the course of their 3-year participation in the trial.

First, children will be enrolled and randomized continuously over an 18-month period. Therefore, children will start the intervention in a staggered way and will not participate along with a given cohort of other children.

Second, the most intensive part of the intervention is the home-based intervention. It is divided up into modules of home environment changes, reducing screen time, reducing energy intake, increasing physical activity, and problem solving, and will be implemented at the individual family level (i.e., not in groups). Families will be able to choose the order in which they receive the modules and they will be delivered by one or more members of our intervention staff who make the home visits (also potentially not static).

Third, children receive their primary care intervention from their own primary care clinician or clinic. Many low-income children represented in this study receive their care at public clinics where they do not have a consistent primary care provider or even a consistent clinic they attend. In our Pilot study, 40 families identified 24 different sources of primary care (many of which were clinics) and one declined to state, at just a single point in time. We also know that many families change their primary care providers over time as their government assistance, insurance or financial status changes over time. Therefore, children in the study will experience

a diversity of different primary care providers.

Finally, while children will have the opportunity to participate in after-school sports with groups of other children, they are allowed to attend any number of afternoon sports sessions (from never to every day), at any one of three to six centers throughout the study period. Thus attendance at a particular center is not static or consistent. In our ongoing Pilot study involving 30 children assigned to after-school sports, the attendance has averaged 61% of possible days (with the number of possible days defined differently for each child) with a range of 8% to 92% over just three months. Our past after-school studies suggest this variability will only continue to grow in a longer study. In addition, while the focus of the afternoon sports sessions will be "team sports," this is not the same as "sports teams." They learn and participate in team sports but are only occasionally grouped into "teams." Children attending on the same day will frequently be broken up into smaller groups to provide more individualized coaching. The membership of smaller groups varies daily or even multiple times per day. Therefore, individual children will experience the after school sports intervention with a very large number of different combinations of children over their three years of participation.

For example, one child may be enrolled at the very beginning of the study but never attend an after-school center, and have home visits by staff members A, B and C, for modules W, X, Y and Z, and attend clinic visits with physician 1 at clinic L and nurse practitioner 3 at clinic M. Another may be enrolled a year later and attend after school programs on Mondays at Center 1, and Wednesdays and Fridays at Center 2 in year 1 but Tuesdays, Thursdays and Fridays at Center 1 in year 2 and 3, have home visits with intervention staff member D, for modules Y, Z, X, W, and attend clinic visits with clinicians 1, 3, and 5.

Thus, it is apparent that identifiable and stable clusters of participants do not exist in our study, nor does our design induce a clustering of subjects where one would expect the errors of responses among certain groups of subjects to be correlated. Therefore, our expectations about our study design clearly indicate the potential risk for correlated errors due to clustering is extremely small, if not zero.

In addition to considering the potential of our study design to induce clustering, we also look at past experience. First, estimating the risk of correlated errors may differ depending on the outcome of interest as well as the nature of the clustering. For example, adolescent smoking or drinking and other more social behaviors might be expected to have more "epidemic" qualities that would translate into clustering of responses than more biological measures, such as BMI, triceps skinfold, and waist circumference, as proposed for this study.[189] Any expectations of correlations for complex, biological measures like BMI would also be more likely among children in the same family than among children attending the same community center. This has been shown emipirically in studies estimating intraclass correlations (ICC) for BMI. This expectation is further reinforced by examining results from our previous studies of BMI change where the design *does* induce clustering of responses. In previous cluster-randomized childhood obesity intervention studies with which the Stanford team has been involved, where the definitions of clusters are clear and often considered to present a greater risk of potential correlation, we have not seen any difference in the standard error estimates whether conducting the analysis assuming independence or accounting for clustering in the model. This suggests that the ICCs for BMI change and skinfold thickness as outcomes are negligible, even in the presence of design-induced clusters. Therefore, our past experiences with BMI in children strongly support our assumption that, even if some level of clustering occurs and we could define those clusters with any accuracy, the expected correlation of responses within some definition of clusters is negligible and will not materially impact the type I error rate. Thus, we consider both context and past experience as guidelines for what to expect and how to best model effects given our study design.

What if our expectations are wrong, despite our experience and expertise regarding our design? Are there potential costs of accounting for clustering in our primary analysis if it isn't

truly there or if we cannot accurately identify the correct clusters? In the development of our analysis plan, one suggestion was to do one's best to model the small group structure in one's data analysis plan and also use empirical sandwich standard errors as an insurance policy against misspecification of that small group structure. However, all models rely on assumptions for statistical validity and therefore pose risks, for example in terms of Type I or Type II errors – even those that make use of robust standard error estimates. There is no free lunch. One cannot just apply robust standard error estimates without paying any price. Under stringent conditions, robust standard error estimators have good statistical properties that allow nominal Type I error rates.[190, 191] For example, under certain regularity conditions, if one were to incorrectly assume an exchangeable correlation structure for the clusters, robust standard error estimators would yield statistically valid estimates. When the conditions are violated, however, these estimators may be biased and inefficient.[192-196] These properties rely on the assumptions of a sufficient number of clusters and that the definition of cluster is clear. While sandwich estimators are robust to misspecification of the model, they are not robust to misspecification of the cluster. We have demonstrated this with simulation studies at both Stanford and Ohio State University (led by David Murray).

Our Stanford studies demonstrate that misspecification of the clustering structure matters, even when the data arise from a sufficiently large number of clusters. The implications of this are a high probability of falsely rejecting the null hypothesis (substantially inflated Type I error rates). We conducted simulation studies for a two-arm study, where the number of clusters, the intraclass correlation coefficient and the sample size varied. We found that robust estimators that assumed clustering of independent data yielded type I error rates of up to 40%. In the presence of true clustering, partial and complete misspecification of cluster membership (where some and no knowledge of true membership was incorporated into assumptions, respectively) produced intermediately inflated type I error rates depending on the ICC and degree of misspecification. Therefore, while robust standard errors may be used to provide protection against misspecifying the correlation structure of clustering, they do not protect against misspecifying cluster membership. In these cases, an OLS model that assumes independence was often found to be at least comparable or superior.

Our study points to the need to make careful and thoughtful assumptions about both the correlation and clustering structure in choosing an analysis strategy for potentially clustered data. If the errors corresponding to subjects' outcomes are uncorrelated, results can be misleading by incorrectly assuming correlation exists. Similarly, even if subjects are clustered and the number of clusters is sufficiently large, results can be misleading if clustering membership is misspecified. In these cases, an OLS model that assumes independence is superior to one that completely misspecifies the structure.

In some cases, one is likely to have some information on cluster membership. Partial misspecification was found to produce lower type I error rates than assuming independence in some cases if the ICC is strong. When the data are weakly clustered in an unclear manner, however, assuming independence produces comparable type I error rates to partial misspecification, provided the design effect is not large. Furthermore, the implications of misspecifying cluster membership can be high. When the ICC is weak and confidence in membership is not high, our findings recommend assuming independence.

The Ohio State University studies examined the situation when each participant is involved in more than one small group at a time. They also found that sandwich estimators performed poorly in this context and recommend against their use. In further simulations, however, they showed that a mixed model can perform well when the small group structure is misspecified, at least in a limited way. In one case, they modeled one small group structure (a) correctly but ignored the other (b) and made use of Kenward-Roger degrees of freedom. This model performed well for any non-zero ICCa when ICCb was 0, 0.001 or 0.01, but not when ICCb was 0.1. Thus, this approach appears to be satisfactory if one expects the ICC in the

ignored cluster to be small. These simulations do not tell us what happens when participants may belong to more than 2 or a variable number of small groups and/or small group membership changes over time (as in the Stanford study), or how the mixed-model performs under more extreme cluster misspecification or when the data are truly independent.

We have designed our analysis plan based on the assumptions that we believe best fit the Stanford study designs and the best available evidence at this time. In summary, (1) knowledge of the design of our study suggest it will not induce correlated responses among children who are participating to various degrees in the various intervention components, (2) past research suggests that ICCs are negligible when children's BMI change is the outcome, even in cluster randomized trials, (3) robust standard errors do not provide an insurance policy against potential non-zero clustering when the cluster structure is misspecified and/or participants are involved in more than one group at a time, and (4) incorrectly assuming clustering in the absence of clustering yields inflated type 1 error rates. Our approach, therefore, is to assume independence of responses across children in our primary analysis. In addition, we include a secondary analysis to address the unlikely potential of non-zero correlation (where cluster is to be defined post-hoc by our empirical data). If our results differ, we will report them. Would a different result mean the analysis accounting for clustering is the correct analysis? Not necessarily. And because we do not know the truth, we cannot say. We have to base our primary results on the model that uses the assumptions we believe are closest to the truth and, for all the reasons above, this is the model proposed in our primary analysis.

11.4.3. Missing data including level of attrition, lost to follow-up, and missing data treatment.

Our primary outcome is a derived measure of change in BMI values for each child. More specifically, change in BMI will be estimated by computing a slope for each child by regressing BMI on time, where each child may have up to 4 BMI measurements (at baseline, 12 months, 24 months, and 36 months post randomization), and by assuming that BMI behaves linearly over time. Children with at least 2 measurements will have a corresponding derived slope. Children with only one BMI measurement at baseline, however, will have missing outcome values. Based on prior studies in low-income, high-risk, community-based samples, we expect less than 5% of the sample will be completely lost to follow-up after randomization and thus have missing outcome values.

Handling of Missing Data and Intent-to-Treat Analysis: We will use multiple imputation (MI) techniques to multiply impute outcomes (slopes) for children without slope measurements (those children with only a baseline measurement) using the fully conditional specification approach of imputation. MI allows inclusion of all children randomized to treatment arm so we can perform an intent-to-treat analysis. The validity of results from applying standard MI techniques relies on the data being missing at random (MAR). While it seems plausible that children with less success or with increasing BMI may be more likely to drop out of the study indicating the data may be not missing at random (NMAR) and violating the assumptions of standard MI, after conditioning on baseline and intermittent BMI measurements, however, it is reasonable to assume the data are MAR. Fortunately, our study design ensures that every child will have a baseline BMI measurement that can be incorporated into an imputation model. Our imputation model will additionally include all variables specified in the scientific model including the outcome variable as well as any potential auxiliary variables, such as gender, intermittent BMI values, race, and any other relevant demographic characteristics. As suggested in Little and Rubin[197] 5 imputed data sets should provide reasonably efficient estimates. If the fraction

of missingness is larger than 15%, however, we will evaluate whether increasing the number of imputed data sets yields point estimates that change by more than 10%. If this is the case, our results will be based on the minimum number of imputed data sets that yields point estimates that do not vary by more than 10%. A sensitivity analysis that varies the imputation model as well as assumptions regarding the missing data mechanism is discussed in the section below regarding secondary analyses.

11.5. Detectable Difference, Sample Size, and Power

Assumptions Regarding Effect Sizes and Standard Errors

The statistical literature recommends against the use of pilot studies to estimate effect sizes for clinical trials.[198] Instead, estimated sample size requirements should be based on the *a priori* minimum acceptable difference between groups to be considered of clinical or public health significance, from the experience and judgment of the investigators.[198-201] In this case, the effects of the MMM intervention compared to the enhanced standard care control condition. Based on our judgment and experience, we estimate this minimum acceptable difference to be an effect size (Cohen's d) = 0.4. This is the equivalent of about 27% non-overlap of two normal distributions, or 50% of one group's distribution being greater than about 66% of the other group's distribution,[202] a Number Needed to Treat for one additional success (NNT) of 4.49, a Standardized Risk Difference (SRD) of .223, and an Area Under the ROC Curve (AUC) of .611.[199, 200]

We can also use the changes observed in our pilot studies to better estimate the effects we expect to achieve in the proposed trial. The 12-week Dance for Health intervention resulted in a Cohen's d effect size = 0.43, the 7-month school-based screen time reduction intervention resulted in a Cohen's d = 0.67, and the 12-week Stanford GEMS Phase 1 Pilot Study resulted in a Cohen's d = 0.42. Therefore, achieving an effect size of 0.4 or greater is certainly realistic, and the MMM intervention strategy, with an increased intervention length and intensity compared to past studies, and starting with an overweight sample, is expected to result in an even greater effect size.

To further aid in interpretation of meaningful effect sizes, we include clinically relevant scenarios that correspond to a Cohen's D statistic of 0.4. This statistic is a function of the difference in average slope for each group and the corresponding pooled standard deviation. Examples of clinically relevant scenarios that corresponds to a Cohen's D statistic of 0.4 include the following:

- Average decrease in treated children is 0.1 BMI units per year while controls increase at a rate of 0.4 BMI units per year with a standard deviation of 1.2.
- Treated children decrease by almost half a BMI unit per year (0.4) while controls have no change in BMI per year with a standard deviation of 1.0.
- Both groups increase in BMI each year where treated children increase by 0.2 BMI units per year and controls increase by 0.6 BMI units per year with a standard deviation of 0.9.

Power Calculations. For a two-tailed 5% alpha level test, the planned sample size of 120 children per group would provide approximately 90% power to detect intervention effects of that magnitude or greater.[201, 202]

Based on simulation studies (1000 simulations per scenario) we have assessed power for detecting meaningful treatment effects in the presence of an interaction between treatment and baseline BMI. The table below presents our simulation study and demonstrates that we have excellent power for detecting clinically relevant differences between treatment arms. Previous studies investigating rate of change in BMI give standard deviation estimates ranging from 0.8

to 1. We consider a wider and more conservative range of estimates from 0.9 to 1.8. For example, in Scenario 1 where children in the intervention group do not increase their BMI, while controls increase by 1.3 BMI units on average, we have more than 95% power to detect an overall treatment effect. Scenarios 10 and 11 demonstrate we have sufficient power (94% and 89%) to detect a treatment effect if children in the intervention group have no change in BMI on average and children in the control group increase their BMI by about a half unit per year. Finally, we have 83% power to detect a main treatment effect if both arms increase in BMI with the treatment group increasing at an attenuated rate relative to controls (0.95 BMI units per year versus 1.3 units on average) (Scenario 12).

Table 11.1. Power simulation scenarios

	Average Slope (SD) by Group					
Scenario	Treated OW	Treated Obese	Control OW	Control Obese	Effect Size (Cohen's d)	Power
1	0.0 (1.8)	0.0 (1.8)	1.2 (1.8)	1.4 (1.8)	0.7	>95%
2	0.5 (1.8)	-0.5 (1.8)	1.2 (1.8)	1.4 (1.8)	0.7	>95%
3	0.5 (1.8)	-0.9 (1.8)	1.0 (1.8)	1.0 (1.8)	0.6	>95%
4	0 (0.9)	-0.9 (0.9)	0 (0.9)	0 (0.9)	0.5	>95%
5	0.2 (1.0)	-1.0 (1.0)	0 (1.0)	0 (1.0)	0.4	87%
6	0.3 (1.2)	-0.5 (1.2)	0.4 (1.2)	0.4 (1.2)	0.4	90%
7	0.5 (0.9)	-0.2 (0.9)	0.5 (0.9)	0.5 (0.9)	0.4	86%
8	0.5 (0.9)	-0.1 (0.9)	0.5 (0.9)	0.6 (0.9)	0.4	87%
9	-0.14 (0.9)	-0.6 (0.9)	-0.1 (0.9)	0.1 (0.9)	0.4	89%
10	0.1 (0.9)	-0.1 (0.9)	0.4 (0.9)	0.4 (0.9)	0.4	94%
11	0.1 (1.2)	-0.1 (1.2)	0.4 (1.2)	0.6 (1.2)	0.4	89%
12	1.1 (0.9)	0.8 (0.9)	1.2 (0.9)	1.4 (0.9)	0.4	83%

11.6. Analysis for Possible Effect Moderators Mediators

As described above, we will sample variables from several domains (i.e. demographic, socio-cultural, psychological, biological) for inclusion in analyses designed to shed light on the potential mediators and moderators of treatment response. Moderators and mediators have long been discussed in the psychotherapy outcome literature.[203-207] However, attempts to conduct formal analyses of mediators and moderators have been less than successful. For example, depending upon choices made by the data analyst, the use of multiple linear regression to identify moderators or mediators often leads to the situation in which factor A may moderate B and vice versa or A may mediate B and vice versa all in the same dataset. Recently, a MacArthur Network project has attempted to clarify the definitions of "mediator" and "moderator"[204] and to extend them.[208, 209]

A "moderator" of treatment is a pre-randomization factor (hence uncorrelated with treatment in an RCT) that has an interactive effect with treatment on a particular outcome. Subgroups of the population sampled in the RCT, identified by strata of a moderator variable, may have different effect sizes of treatment. Moderators are useful to allow appropriate targeting of treatment, as well as in research to identify appropriate inclusion/exclusion criteria in future studies, or factors on which a study should be stratified to amplify power. To show that a pre-randomization factor is a moderator of the treatment effect on treatment outcome, we will examine treatment, the putative moderator and their interaction as the independent factors. Since, in a randomized clinical trial, the treatment assignment is independent of all pre-

randomization factors, these factors are orthogonal in the model. Thus, the overall treatment effect will not change from that of the primary analysis. What we are seeking here is either a main effect or an interactive effect of the putative moderator. A statistically significant interaction is indication of a moderator effect.

11.7. Analysis for Possible Effect Mediators

A "mediator" is a post-randomization event or change during treatment that is correlated with treatment (thus possibly an outcome of treatment), and that has either a main or interactive effect with treatment on the outcome of interest. If there is a causal chain linking treatment with outcome, then the links of that causal chain are "mediators." While all links of such a causal chain are mediators, not all mediators are links of a causal chain. Mediators, however, are useful in giving clues to what direction might be most profitable in the search for causal chains. To show that a post-randomization factor measured during treatment is a mediator, one must first demonstrate that this factor is itself an outcome of treatment, i.e. that it is correlated with treatment. If this factor is significant, but not totally collinear with treatment, it would be used in an analysis as above. Either a main or an interactive effect of the factor with treatment would indicate a mediator role of the factor. Moderator and mediator analyses are necessarily hypothesis-generative secondary analyses following the hypothesis-testing analyses that define a RCT. They are, however, both necessary and valuable, in that they increase our understanding of the primary results of the trial, thus providing guidance to appropriate clinical and public health application. Moreover, the information gained is invaluable in conceptualizing and designing cost-effective future trials.[208-210]

11.8. Secondary Hypotheses and Analysis.

Further Characterization and descriptive analysis of the primary outcome:

Following the primary analysis we will perform additional descriptive analyses to better characterize the clinical significance of the results. For descriptive analyses, effects are characterized not by statistical significance but by judgments of clinical significance. In this analysis we will examine treatment effects based upon thresholds of BMI. For example, we will plot the risk ratios associated with having a BMI change greater than a specified threshold at the study endpoint defined by the CDC 2000 BMI standards for age and sex.

Changes in waist circumference and triceps skinfold thickness will also be assessed to further characterize changes in adiposity resulting from the intervention.

Secondary Hypotheses:

Compared to standard care/health education controls, children randomized to our multi-component, multi-level, multi-setting (MMM) intervention will have significantly greater trajectories of physical activity (objectively measured by accelerometers) and HDL-C, and significantly attenuated trajectories of waist circumference, triceps skinfold thickness, resting systolic and diastolic blood pressures, resting heart rate, fasting Total Cholesterol, LDL-C, TG, Insulin, hemoglobin A1c, hsCRP, ALT, screen time and other sedentary behaviors, average total dietary energy intake, weight concerns, and depressive symptoms.

Analyses of Secondary Outcomes:

We will use a similar analysis approach as used with the primary analysis to examine the effects of the intervention on all secondary outcome measures.

11.9. Additional Analyses

We will present descriptive statistics such as means and medians for continuous variables and frequency tables for discrete and categorical variables. Graphical techniques such as histograms and QQ-plots of outcomes will be used to assess distributional assumptions.

Success of Randomization/Description of Population/Effect of Attrition:

To verify the success of randomization and the comparability of the two experimental groups, we will compare baseline measures of the treatment arms. Descriptive statistics from these analyses will also define the population to which the results may be readily generalized. We also will assess the loss of subjects (attrition), comparing the treatment and control groups, and comparing baseline responses of "completers" with those who are lost.

Correlate/Risk Factor Studies:

We will use mixed effects linear regression techniques to describe individual trajectories of change over the course of the study, and then step-wise regression tools to identify the factors predictive of different response patterns, as well as signal detection methods[211] to identify discrete subgroups.

Process/Delivery of Intervention Studies/Success of Intervention Studies:

Using similar statistical tools for modeling and model selection, we will use process measures to assess the intervention implementation and describe the processes by which the intervention might be more or less successful, to gain a better understanding of the implementation and how to improve it.

Sensitivity Analyses

Comparing BMI trajectories over time between intervention groups:

A secondary aim is to address whether trajectories of BMI over time (that may be non-linear) may differ between treatment arms. We address this in our secondary analysis through use of a mixed effects linear regression model that includes a child-specific random intercept. In this model we will make use of all the individual BMI measurements within a child. We allow BMI to behave non-linearly over time by fitting and evaluating three possible models: one where the four time points are represented by three indicator variables, one where a linear and quadratic term are included, and one where a linear, quadratic, and cubic term are included. Model selection among these three choices will be done using the likelihood ratio test. Product terms between time and treatment group will be included in each model, as the parameters representing these interaction terms are of interest and represent the differential trajectories of BMI over time across treatment arms. For example the first model can be written as:

$$BMI_{ij} = beta0 + gamma_i + beta1\ treatment_i + beta2\ time2_{ij} + beta3\ time3_{ij} + beta4\ time4_{ij} + beta5\ treatment_i \times time2_{ij} + beta6\ treatment_i \times time3_{ij} + beta7\ treatment_i \times time4_{ij} + epsilon_{ij}$$

where BMI_{ij} is the BMI measurement for the i^{th} child at the j^{th} visit, where j=1,2,3, or 4, $gamma_i$ is the child-specific random intercept term assumed to follow a normal distribution, $epsilon_{ij}$ is the random error term corresponding to the i^{th} child at the j^{th} visit. Such a model allows flexibility in how BMI behaves over time. Our hypothesis of interest is whether the trajectories differ. This involves testing whether beta5=beta6=beta7=0.

Sensitivity analyses of primary findings to assumptions of independence:

One secondary analysis is to assess the impact of assumptions regarding independence of errors across subjects in the primary analysis, as discussed above. To that end, we will repeat the primary analysis applying a mixed effects model to assess whether treatment impacts BMI change after accounting for potential clustering of responses. Appropriate clusters will be defined by examining patterns of after school community center attendance and other intervention features such as home intervention staff and primary care professional/clinic. These will likely be a function of both pattern of community center attendance, primary care professional/clinic utilization, and home intervention staff (e.g., no after-school center attendance with home visits by staff members A and B and clinic visits with physician 1 and nurse practitioner 3; mostly Center 1 after-school attendance with home visits by Staff Members A and B and primary care at clinic 3, a mixture of after-school Centers 1 and 2 attendance with Staff Member C and clinicians 1 3 and 5, etc.) We do not expect this analysis to be different from the primary analysis. If it does differ, however, we will report the discrepancies in a secondary analysis.

Sensitivity analyses of primary findings to assumptions of missingness:

Our primary approach involves actively imputing the slopes for only those individuals with no follow-up visits. An alternative approach that we will consider involves imputing BMI values for all individuals missing any follow-up visits and then subsequently deriving slopes. The latter is known as passively imputing the outcome. Under both approaches (the active and the passive) we will assess the sensitivity of our results to assumptions about missingness. More specifically, in addition to considering multiple models under the MAR assumption, we will also consider MI models under the NMAR missing data mechanism. Varying the imputation methods and the assumptions about the missing data mechanisms allows us to gain insight into the robustness of our findings across assumptions. A nice feature of MI is that we can average over the uncertainty of these assumptions. All assumptions considered will be incorporated into a summarized finding (i.e., averaged over into one final model). The array of results, however, will also be presented to give the reader a sense of the robustness of our findings in the event that different assumptions lead to markedly different results and the uncertainty of our final results will be quantified and described.

12. DATA MANAGEMENT & QUALITY CONTROL

12.1. Common Database

The COPTR Data Center was designed after extensive discussions with representatives from all of the sites to provide a secure, easy, and effective set of tools for submitting Common Measures to a central repository for the consortium. Each of the four Field Sites has a site-specific data system for conducting the daily tracking and data collection.. The COPTR Data Center does not dictate how those disparate site systems are designed or used. Instead, the Data Center provides a set of web-based tools for sites to upload completed Common Measures to the central repository at the RCU.

Field Sites collect a subset of the Common Measures following the protocols and manual of procedures (MOPs) for those common measures. The common measure subsets for each Field Site differ slightly but the MOPs and protocols defining the measurement/collection procedures are identical. The recruitment data elements identified for submission to the RCU are identical at each Field Site. Each Field Site submits the current collection of common measures quarterly and the recruitment and retention data monthly to the RCU to be included in the central data store of the Consortium. Variables collected at only one Field Site are not transferred to the RCU.

One or more representatives from each Field Site have been designated as members of the Data Capture Working Group. These representatives contributed to the design of the Data Center tools and continue to contribute to improved functionality of the Data Center site. These representatives also serve as the primary contacts at a Field Site when the RCU notices irregularities with the submitted data.

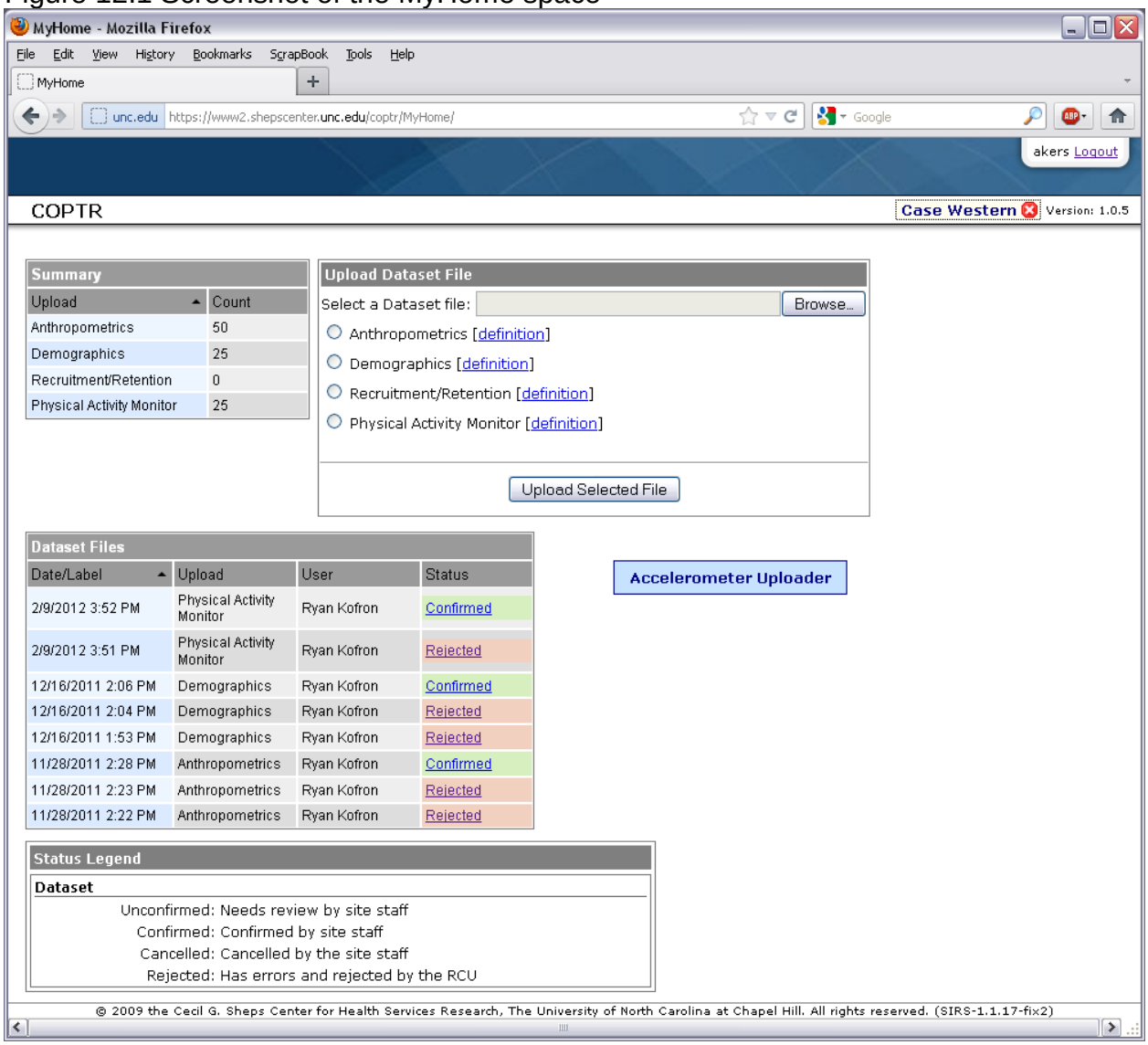
The RCU data transfer system utilizes a restricted access website to provide encrypted transfer of data files containing common measures (measurements collected at more than one Field Site) to a central data repository at the RCU. Each Field Site will have one or more project staff authorized to have access to the Data Center website. An individual at a site must receive authorization from the site's PI prior to getting an assigned Data Center userid and password. Field Site staff login to the Data Center via the following URL:
http://www.shepscenter.unc.edu/coptr

After successful authentication, the user will land on the "MyHome" page of the affiliated Field Site. Access is restricted according to Field Site affiliation and defined roles. An authorized staff for a Field Site only has permission to work within that site's defined workspace. Some RCU staff are authorized to work across all Field Sites' workspace. Figure 12.1 is a screenshot of the Case Western MyHome space.

On this MyHome page, a Field Site user (e.g. Case Western user) will see two sections that give real-time information on successful uploads and attempts. The top left box provides a Summary of the data records by type that have been uploaded to the Data Center and Confirmed by any of the site's authorized users. The Dataset Files box just below the Summary box provides more detailed information on each upload attempt. Authorized site users always have access to these status displays. Furthermore, authorized RCU users can see the status displays of all four Field Sites, providing an opportunity for RCU staff to monitor upload processes and provide assistance when errors are displayed. In addition to the MyHome

displays, the Data Center system has extensive error logging available to RCU staff to troubleshoot any problems encountered. Last, to the right of the Summary box are the tools for uploading data sets.

Figure 12.1 Screenshot of the MyHome space



Data Capture and Data Audits

Uploading Data to the RCU

The COPTR Data Capture Working Group decided to use file upload facilities versus web data entry forms for submitting site data to the Data Center. To upload a data set, the user will Browse his/her local file space for the desired CSV file, select the corresponding type by clicking on the appropriate radio button (e.g. Anthropometrics, Demographics, etc.), then click “Upload Selected File”. The upload process evaluates the incoming data file, looking for the required

unique identifiers, the correct site ID, and comparing the field names, data types, and data values according to the predefined “definition”. (The “definition” files are available to read via the “definition” links.) If any required data check fails, the RCU rejects the incoming file and reports the reasons to the user. The user can then correct those issues and upload the file again. If all required data checks pass, the incoming file is held with “Unconfirmed” status and the user is presented a report on the number of new records and number of modified records found in this incoming file. This report provides the user an opportunity to confirm that those numbers are as s/he expects. If the numbers are as expected, the user can “Confirm” the upload and the process is complete. Otherwise, the user can “Cancel” the upload then investigate the issues offline and attempt the upload again at another time.

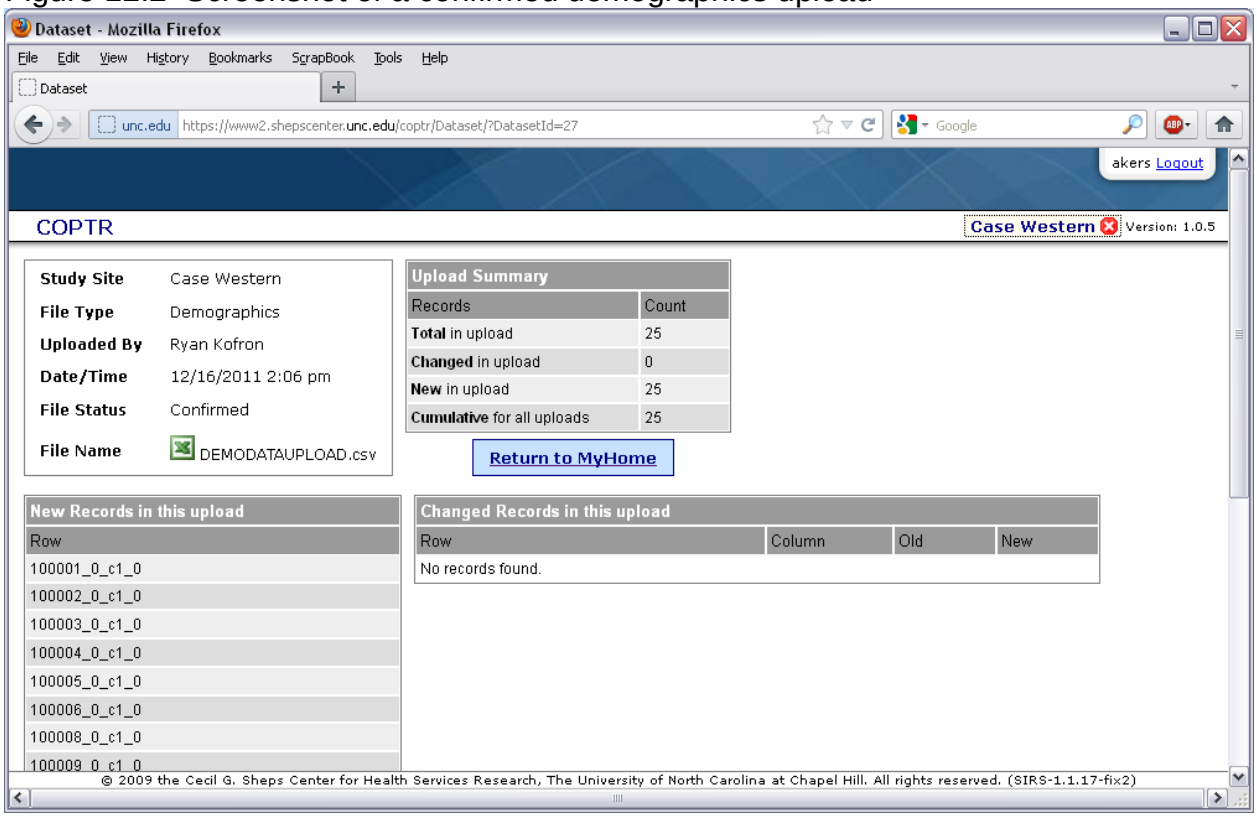
The next section on the screenshot in Figure 12.1 shows a running log of the dataset upload activities for the site. The log shows the date and time of each upload attempt, the type of upload, the user performing the upload, and the status of that upload attempt. Clicking on a “Confirmed” link in the Status column loads more detailed information about the confirmed upload. Figure 12.2 shows the details of a confirmed Demographics upload from Case Western. The more detailed information includes the local File Name of the uploaded file, the Upload Summary, and the unique identifiers of the New Records that were included in that file. In addition, if there were records uploaded that were intended to update or correct data that had previously been uploaded to the RCU Data Center, details of those changes would be listed in the right hand table labeled “Changed Records in this upload”. Changes to data fields in existing records are made by matching the unique record key of an existing record with that of an incoming record then accepting the new incoming record as the most up-to-date. (The older record is kept for reference. It is not overwritten.)

The Data Center is designed with three objectives in mind:

1) Promote the submission of the highest quality data to the RCU for future use of the Common Measures;
2) Provide an upload facility that is efficient and easy to use from the individual site’s perspective;
3) Give the users enough information and flexibility to track progress and correct problems with Common Measures submissions.

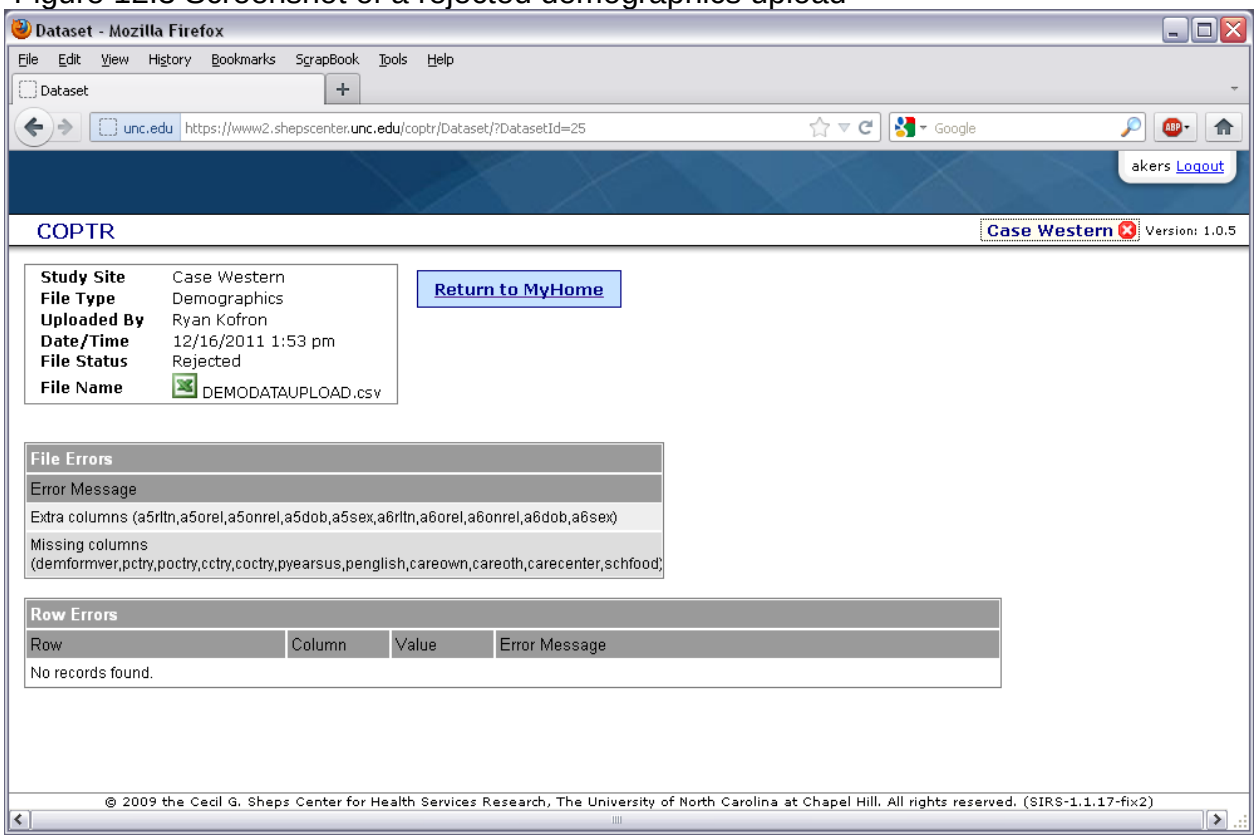
To that end, all data uploads with the exception of the accelerometer GT3X or AGD uploads, follow the same general model: organize your data to fit the approved definition, upload a CSV file via the website, confirm the upload or correct the errors and try again. Figures 1-3 illustrate the information provided and assistance with identifying and correcting problems prior to the RCU accepting data.

Figure 12.2 Screenshot of a confirmed demographics upload



Clicking on a “Rejected” link in the Status column will load more detailed information about a file with data that did not match the required criteria for acceptance in the Data Center. Figure 12.3 below shows the details of a rejected Demographics upload. Again, the local File Name is displayed along with Date/Time and Uploaded By user. The File Errors box in this example indicates that an upload was attempted that contained extra fields that the RCU was not expecting (first message). Also, the second message indicates there are fields or columns missing in the upload that are required as Demographics Common Measures. If there had been any data type mismatches or data values out of range, error messages would be presented in the “Row Errors” box.

Figure 12.3 Screenshot of a rejected demographics upload



Authoritative ID File – Study Arm

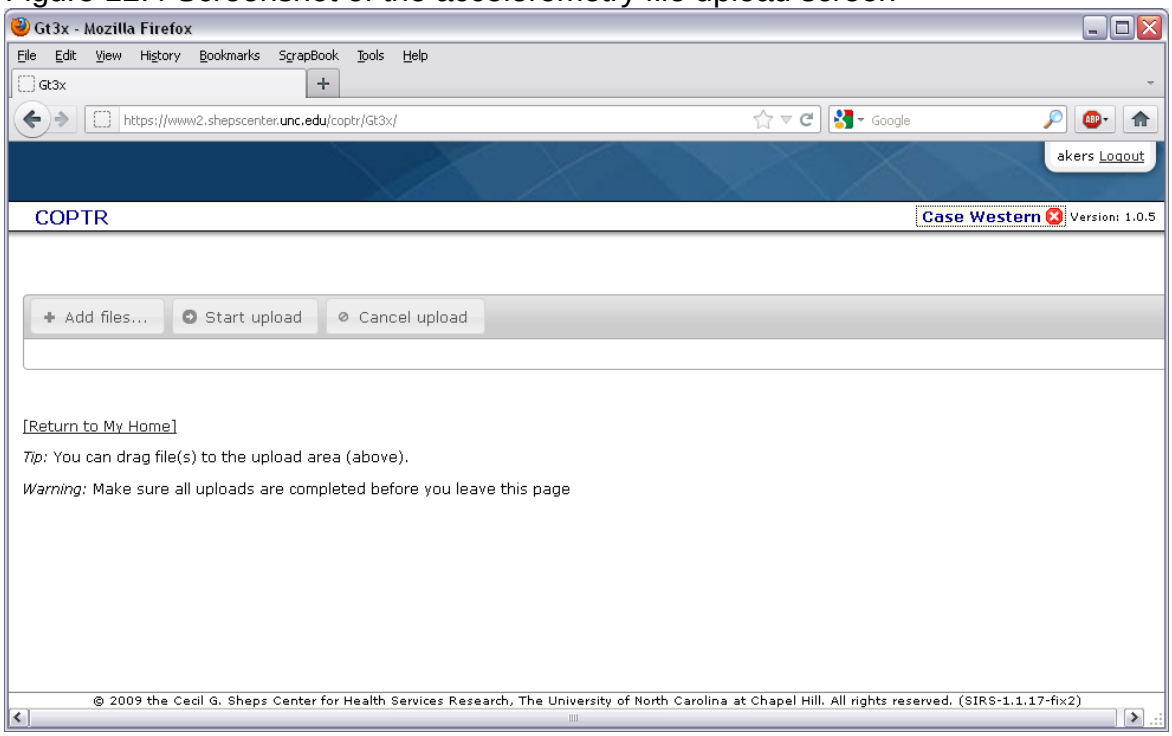
The RCU Data Center requires one of the data uploads to be the authoritative source for Index Child IDs. Having an authoritative "master" list of Index Child IDs allows the RCU to prevent orphan records from being introduced in any of the other data uploads. The consortium has designated the Study Arm upload to be this source. As such, a Study Arm record for an Index Child must be uploaded to the RCU before any other Common Measure records are accepted into the Data Center. The Index Child IDs in other data uploads (e.g. Anthropometric, Demographic, etc.) are verified against the RCU's Study Arm records prior to accepting the data records. Data records that do not have a matching Index Child ID in the RCU's Study Arm data are rejected to prevent orphan records from being introduced into the Data Center.

Accelerometer Data

Accelerometer data on an individual consists of two distinct parts: a Physical Activity Monitor (PAM) record, and recorded data from the ActiGraph device (GT3X or AGD format). The RCU requires sites to upload the PAM record of the pair prior to uploading the matching GT3X or AGD file. The steps for uploading PAM records follows the same steps described above for other data uploads. However, the steps for uploading GT3X or AGD files are different because of the difficulties introduced in handling these large files. (We are anticipating the average size of these files to be around 200MB.) After successfully uploading and confirming PAM records, the user clicks the "Accelerometer Uploader" button shown in Figure 12.1. The user is then presented with a screen similar to Figure 12.4 below. The user can then queue up one or more GT3X/AGD files for upload either by clicking "Add files…" or by dragging files from local file space into the upload area. Clicking "Start upload" will begin uploading the queued files in the

order they are shown. Each GT3X/AGD file is verified against the uploaded PAM records to ensure a PAM record exists for a GT3X/AGD file before allowing the upload to proceed. This verification allows the RCU to accurately link a PAM record to an incoming GT3X/AGD file. The user must make sure all queued uploads are completed before leaving this web page.

Figure 12.4 Screenshot of the accelerometry file upload screen



Uploaded GT3X and AGD files are not automatically analyzed at the RCU. The files are simply stored in a file system for later use. Each site is responsible for analyzing GT3X and AGD files for completeness prior to uploading to the RCU Data Center.

12.2. Site-Specific Database

Physical data measures for both children and adults are entered directly into a customized FileMaker database system which is set to prompt the data collector to follow all MOP rules, including rules as to when a 3rd physical measure is needed or if the measurement needs to be checked as valid.

The database is designed to prompt data collectors when to perform test-retest measures and, unbeknownst to the data collectors, will additionally prompt a height re-measurement when a child participant is measured as shorter than at a previous visit or and adult is measured more than .5cm shorter than a previous visit.

Child survey measures will be directly entered into the same database, using similar systems to make sure all questions are answered and within expected ranges, to prevent transcription errors.

Once the baseline visit record is complete in the database it is locked to prevent any further manipulation and can only be unlocked by the database manager and data aide in order to be modified.

Parent surveys will be completed on paper. To ensure data completion, paper surveys are reviewed once in the field and again in the office before being sent to an outside keypunch company which double enters all data. Once data are returned, data are built into SAS databases and at least 20% are reviewed for accuracy by staff data aide.

The data team meets weekly to review visit progress and ensure that all visits are being completed as expected. Each overdue visit is reviewed and any visits not fully completed within 30 days are reviewed. Questions and concerns are raised with the Principal Investigator as needed.

Data reports, including completeness and range and frequency for categorical measures and range and mean (sd) for continuous measures are reviewed at least monthly and typically bi-weekly by the database manager and principal investigator.

Data will be uploaded quarterly to the RCU as directed by the MOP.

In addition, we include these general approaches for quality control in data collection and data management, prior to database management.

- All measures are made according to a detailed MOP
- Updated protocols and MOP are kept both online and in hard copy binders for easy access
- Training is conducted using step-by-step instructions and data collectors meet weekly throughout the study to share experiences and problem solve, if necessary
- Data collectors must pass certification prior to collecting data
- Protocols are followed for physical measures instrument validity/calibration checks
- Inter-rater reliability is assessed throughout the study on a randomly 10% of participants
- Ongoing (booster) trainings are provided throughout the study
- Data collectors use checklists for each visit to ensure completeness
- Any paper surveys are color coded
- ID labels are preprinted

- IDs include a last digit as a check digit
- Direct entry of most data (custom filemaker pro database) to reduce transcription errors and eliminate readability errors
- Automated real-time safeguards to prevent illogical data entry (e.g., range checks, longitudinal checks)
- Data entry software conducts all calculations in real-time (e.g., eligibility, outliers)
- Double entry of paper survey data
- Standardized data cleaning rules
- Manual and automated checks for completion of all measures
- Tracking of all data in database
- 24-hour recalls – quality control checks on outliers
- Actigraph – immediate download and review for completeness upon receipt
- Color-coded alerts in Filemaker Pro data management system
- Data backed-up on external USB drive at each visit
- Database backed-up daily on remote server

13. SITE SPECIFIC TIMELINE

March 2012 – July 2012	Completion of Phase 1. Completion of Pilot Study post-test assessments, intervention and measures revisions, finalize common and site-specific protocols and MOPs, recruitment of additional staff and training and certification, direct data entry/database software completed.
June 2012 – Dec 2013	Phase 2 recruitment
July 2012 – Jan 2014	Screening, baseline assessments, and randomize 240 families
Aug 2012 – Jan 2017	36-month interventions and 12-, 24- and 36-month follow-up assessments (ongoing quality assurance, DSMB mtgs)
Feb 2017 – Sep 2017	Final QA reviews completed, database locked, data analysis and project closeout, prepare papers for publication, prepare for dissemination of study results and intervention materials

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