This Clinical Trial Protocol contains the following items:

1. Original protocol, revised protocol, and a summary of all amendments.

2. Original statistical analysis plan, final statistical analysis, and summary of all amendments.

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Original Protocol

Specific Aims

This research includes one primary and five secondary specific aims:

Primary Aims:

1. **Aim 1:** Evaluate the efficacy of a multi-level intervention, addressing nutrition and physical activity, at public community recreation centers with high-risk parent- preschool child (ages 3-5) dyads to promote pediatric obesity prevention.
   1.1. **Hypothesis 1**: The BMI trajectories of children in the treatment group will accelerate at a slower rate than those in the control group over time.

Secondary Aims:

2. **Aim 2:** Compare the effect of the intervention in children whose parents made significant changes in their dietary and/or physical activity behaviors to the effect in children whose parents did not.
   2.1. **Hypothesis 2:** Relative to children in the control condition, children participating in the treatment condition will:
      2.1.1. Have lower sedentary activity levels (as measured by actigraphy data) after the intensive phase of the intervention (T2) and at study completion and
      2.1.2. Have better adherence to age-specific USDA nutrition recommendations, (e.g., age-appropriate total calories increased fruits and vegetables, decreased sugar sweetened beverages [measured via diet recall data]), after the intensive phase (T2) and at study completion.

3. **Aim 3:** Evaluate the effect of parents' physical activity levels and dietary behaviors on children's levels of the same.
   3.1. **Hypothesis 3:** Parents who have significantly lower sedentary activity levels (compared to baseline) after treatment and who have better adherence to USDA nutrition recommendations (age-appropriate total calories increased fruits and vegetables, decreased sugar sweetened beverages [measured via diet recall data]) will be more likely than parents who have higher sedentary activity levels and who do not adhere to USDA nutrition recommendations to have children who will show
      3.1.1. Decreased sedentary activity levels post-treatment and
      3.1.2. Better adherence to USDA nutrition recommendations (as measured in 2.1.2, above)

4. **Aim 4:** Explore the potential for developing new social networks and their effect on child nutrition and physical activity.
   4.1. **Hypothesis 4:** Parents in the treatment group will develop new social networks and the strength of those social networks will be positively associated with reduced sedentary activity levels and improved dietary behaviors (measured as indicated above) among both parents and children.

5. **Aim 5:** Evaluate the moderating relationship between genetic risk factors and child BMI trajectories over the course of the study.
   5.1. **Hypothesis 5:** Higher levels of child genetic susceptibility to obesity (i.e., a higher genetic risk score)[1] will be significantly associated with heavier-for-age BMI at baseline, and this susceptibility will moderate children's growth in BMI over time.

6. **Aim 6:** Assess the degree to which implementation of the GROW program encourages additional lifestyle programming for preschool children and their parents in the Metro Community Centers.
   6.1. **Hypothesis 6:** The two Metro Community centers participating in the GROW trial will implement a higher number of activity and or nutrition programs for families (as defined by the centers) with young children at the end of the study compared to non-participating Metro Community Centers.

Background

Early childhood is a critical time for obesity prevention.

Changes in physical activity and diet, among many other factors, have contributed to epidemic levels of childhood obesity in the U.S.[2-6] Obesity rates have tripled among children and adolescents over the past thirty years[7,8], with Latino and African-American populations at disproportionately higher risk.[4,8,9] At the current rates of childhood obesity, 30 to 40% of today's children may eventually develop type 2 diabetes and reduce their life expectancy.[10] Nader et al demonstrated that children who were ever overweight during the preschool period were five times as likely to be overweight adolescents.[11] And the chances of overweight increases as the child ages. In that same study, 80% of school-age children who were ever overweight during this period went on to become overweight adolescents. The significance of mounting risk for sustained overweight and its consequences cannot be overstated. In the Harvard Growth Study, overweight adolescents as adults had a two-fold increase in all-cause mortality and an increased morbidity due to cardiovascular disease.[12] It is not merely overweight/obesity in childhood that poses the risk for later increased mortality and morbidity as an adult, **the slope of early weight gain is a potent predictor**.[13,14] For example, Leunisson et al showed that rapid weight gain without concomitant growth in height during the first three months of infancy is linked with reduced insulin sensitivity in early adulthood. **Furthermore, Barker et al demonstrated that the risk of adult coronary events was more strongly related to the rapid childhood gain in BMI than to BMI attained at any particular age.[13] Consequently, this proposal will address prevention of rapid BMI gain during early childhood, fostering normal growth for those children who have a normal BMI (>50% and <85%) and improving BMI trajectories for those children who already have a BMI ≥ 85% <95% at ages 3-5 years.** There is little evidence documenting successful behavioral interventions to *prevent* early childhood obesity[15-17] and even less evidence concerning which factors may be crucial to success. Consequently, the Institute of Medicine (IOM)[18,19] and the *Strategic Plan for NIH Obesity Research*[20,21] call for a community-engaged, culturally-relevant, family-centered approach to obesity prevention that can be sustainable.

Family plays a crucial role in pediatric obesity prevention.

Family influences normative expectations of how and what to eat as well as how often to be physically active.[22,23] Moreover, families control the home environment that shapes children's early childhood choices, establishing behavioral habits.[24] For example, in the Viva La Familia study, random 24-hour dietary recalls of almost 1000 children showed that 67% of children's meals occurred at home and that most of these meals were high density, low nutrient foods, consistent with their parents' choices.[25] Parental involvement in programs to reduce overweight in children has been moderately successful, and is considered an important component of weight loss programs targeting children.[26,27] Many of these programs were focused on treatment, however, the same association appears to exist for prevention efforts as reported in a recent meta-analyses of randomized trials to prevent childhood obesity.[28] Parents' role appears to be as both models to their children and as active participants in creating a healthy environment that encourages healthy lifestyles. Children are nearly six times more likely to be physically active if their parents are physically active.[29]

One important component of parental involvement is the use of behavior change methods such as parent-child contracting to set clear goals for nutrition and activity and self-monitoring of caloric intake and activity.[27,30] Epstein's report of 10-year treatment outcomes for obese children indicates long-term success among families who used parent-child contracts to set clear goals.[27] In a 2006 position paper, the American Dietetic Association (ADA)[31,32] recommended that effective, developmentally appropriate pediatric obesity interventions include the following elements:

1) Parent training/modeling (involving behavioral counseling targeted at parents to improve their parenting skills);
2) Behavior modification training (involving goal setting, modeling, and self-monitoring);
3) Promotion of physical activity (including the reduction of sedentary behaviors); and
4) Nutrition counseling/education (including the provision of more general information on foods, shopping, and nutrition to promote healthful eating).

Obesity is impacted by both the physical and social environment.

It is not only the family that exerts influence over preschooler nutrition and physical activity habits, but both the physical and social environment.

Physical Environment: A developing area of research examines the impact of access to physical activity on increased activity levels. In a study by Wilson et al, access to physical activity such as neighborhood trails was associated with increased physical activity in low SES groups.[33] These same groups tend to have a higher likelihood of obesity.[34] Likewise, Sallis et al discovered that proximity of exercise facilities to one's home was associated with increased amounts of exercise.[35] Unfortunately, more physical activity barriers exist for residents living in poorer communities. For example, Estabrooks found that fewer free physical activity resources, such as parks and playground exist, in poorer communities.[36] Lack of affordable, safe, and accessible recreation facilities and programs have been cited as contributing to children's watching more TV at home, which in turn is associated with increased rates of obesity.[5,37] Creating links to free, accessible recreation would be especially important in areas where low SES populations live. **Public community centers provide access to physical activity for those populations at highest risk for obesity. Through our existing partnership between the Department of Pediatrics at Vanderbilt University Medical Center (VUMC) and Metro Parks and Recreation, we have the opportunity to conduct and test a community center based intervention that can reach this high risk population.**

Social Environment: Research now suggests that we have underestimated the influence of the social environment on shaping obesity-related behaviors. Social networks have been linked to obesity in adults and adolescents.[38-41] From a recently completed afterschool intervention (Gesell PI), we have initial support for our approach to spread physical activity through a newly developed network. Results indicated that children's existing friendships heavily influenced their routine level of physical activity. The strongest influence on the amount of time children spent in moderate-to-vigorous activity in the afterschool hours was the activity level of their immediate friends. Children consistently made adjustments to activity levels of 10% or more in order to emulate the activity levels of their peers (OR=6.89, p<.01). The child's own age (OR=.92, p<.10) and obesity status (OR=.66, p<.10) had statistically significant but relatively small direct effects on the individual's activity level. Gender had no direct effect on activity.[42] In another recently published study, we found that a new social network evolved among parents enrolled in a community-based obesity prevention RCT: Parents selectively formed friendship ties based on child BMI z-score, (t=2.08, p<.05), thus revealing the tendency for mothers to form new friendships with mothers whose children have similar body types.[43] Together, this work supports our proposition of utilizing the social influences of social networks that form during our intervention to amplify obesity-preventing behavior change. In the GROW intervention we will build new social networks through: frequent contact and facilitated interaction in structured small group activities.

Although the terms are often used interchangeably, social networks differ from social support. Social networks, the complex webs of social relationships and social interactions that connect individuals, have been shown to be strong influences on behaviors. Social support, however, is generally thought not to influence behavior, but rather be a mechanism to cope with challenges and facilitate recovery from illness, injury or disease.[44] Methodologically, social support is measured from the respondent's perspective to assess the support (e.g., emotional, cognitive, tangible support) an individual perceives to have, whereas social networks typically measure the presence or absence of friendships and task- or work-oriented relationships (which may or may not provide support) and treats the ties themselves as objects of study.[45] Social network analysis allows us to see the whole group of individuals and their interconnectedness, and is in that sense broader than analysis of social support. Due to a dearth of data and to methodological challenges, there are fewer studies of how social networks affect health.

Genetic factors play a role in the development of obesity.

New research demonstrates a genetic risk score (GRS) is a potent predictor of BMI. Family studies have demonstrated that genetic factors account for anywhere between 40% and 70% of the population variance in BMI for individuals with severe obesity.[46,47] Until recently, specific genes contributing to BMI in the general population had not been identified. It is now clear, however, that certain gene variants exert a substantial, clinically important effect on BMI in humans.[48] The GIANT Consortium recently reported the results from large scale studies to identify genetic variants contributing to the risk of obesity in both children and adults. In January 2009, this consortium reported a meta- analysis involving over 100,000 patients, in which 8 obesity-related risk alleles were conclusively validated far in excess of the standard (5 x 10-7) for genome-wide statistical significance.[48] Moreover, whereas each particular obesity susceptibility variant confers only a modest effect on BMI, a genetic risk score summing each individual's number of susceptibility variants across all 8 genes is a more potent predictor of obesity.[48] Table 1 below provides the details of the validated genetic associations, specifying the effect of each variant (allele) on BMI. All of the genes are on different chromosomes (unlinked), and therefore, were treated as an independent variable. Given that humans have two copies of every autosomal gene, each person has 0, 1, or 2 risk alleles at each locus, with a

genetic risk score (GRS) ranging from 0-16 (for 8 genes, given 2 alleles per locus, maximum score is 16). Even in the general population, at the extremes of GRS, BMI ranges from 25- 27 are clearly associated with clinical obesity. A novel aspect of the present proposal is that it incorporates genetic data in relation to an interventional study to prevent early childhood overweight/obesity. It has now been conclusively demonstrated that specific genes predispose to obesity, yet their impact on early obesity prevention has not been studied. This critical question must be answered in order to translate the findings of genetic studies effectively into clinical practice.

Prevention must occur in preschool given that 60% of overweight preschoolers will go on to become overweight adolescents.[11] By conducting and testing trials in public community centers, exportable interventions could result allowing for a macro-level system change to address this expanding public health crisis. **Building on the success of an existing partnership between Vanderbilt Pediatrics and Metro Parks and Recreation in Nashville, TN, the team in this proposal will conduct and evaluate an intervention intended to prevent obesity in preschoolers in an approach that affects multiple levels of risk and is both family-based and community-centered. This research includes the following innovations:**

1. Evaluates the trajectory of early BMI gain, as directed by recent scientific discoveries.[13,14,49]
2. Conducts a pediatric obesity prevention trial based in public community centers that are routinely available to the populations at highest risk.
3. Addresses obesity in the understudied period of early childhood – when there may be an optimal opportunity to instill long term healthy lifestyles and BMI trajectories.
4. Assesses the macro-system level components of community centers and social networks and the micro-system level components of parent-child genetics on pediatric obesity prevention
5. Is an easily exportable intervention, and we are actively exploring the opportunity to do so with the National Association of Counties and the National Recreation and Parks Association.

Recruitment

We will recruit 600 adult parents-preschool child dyads (p/c dyads) to participate in this study for 3-years in duration ***(see appendix B for recruitment script)***. To help manage flow of participants at our community center and library performance sites, our sample (n=600 p/c dyads) will be broken down into 3 cohorts of 200 p/c dyads each. ***See Table 1 for breakdown of cohort study implementation design.*** Therefore, recruitment efforts will be on-going every year for the first 3-years to actively recruit 200 p/c dyads for each cohort (n=200 p/c dyads per cohort). In order to preserve internal and external validity of the study, the success of any behavioral intervention is contingent on the researcher's ability to recruit and retain study participants. Successful retention of this longitudinal study begins at recruitment.

Recruitment efforts consist of a multi-pronged strategy including: site- specific recruitment at community pediatric clinics, WIC offices, Family Resource Centers and Read to Succeed sites; study announcements on English and Spanish radio programs ***(see appendix D for invitation letter, language and scripts will be based from this letter)***; and bilingual study recruitment flyers ***(see appendix C for recruitment flyers)*** located at neighborhood organizational centers, Walmart, and other community agencies where families with young children gather (e.g.,

daycares, pre-K programs, churches). In addition to our passive approach, we will also actively recruit in these other community agencies where families with young children gather. In addition, we will identify “community liaisons”, well-respected persons considered deeply integrated in the community who have knowledge and relationships to easily reach and effectively communicate with our target population. Specifically, we will employ 3-6 community liaisons from each of the two communities (Northeast and South Nashville) to aid in recruitment and retention activities.

In order to assist in recruiting our hard-to-reach target population, we will also use Facebook as a viable tool for recruitment. Specifically, we will create a study-specific GROW Facebook page open to the general public that will serve as an online advertisement. All wording and language used for this Facebook page will be similar to our hardcopy flyers that will be disseminated in the community ***(see appendix C for recruitment flyers)***. This page will give interested participants the opportunity to message research staff who can then schedule a follow-up phone call or meeting. Research staff will also have an opportunity to post status updates on upcoming recruitment efforts, for example radio announcements or upcoming community-based events related to the GROW study. Facebook features such as the “like” feature will be enabled whereby individuals that choose to “like” the GROW study page will be updated via their newsfeed (the center column of an individual’s homepage – a constantly updating list of stories from people and pages that they follow on Facebook) whenever our Facebook page updates our status. When individuals “like” this page, it also appears in their respective network’s newsfeeds, thereby potentially exposing the GROW page to other prospective participants.

From our GROW formative research pilot (IRB No. 100591), out of 439 parent/child dyads assessed for eligibility, only 50 parent/child dyads were eligible and participated at baseline; a 10% return on investment. Due to the challenge of enrolling in a large, longitudinal, community-based, prevention trial, another strategy of recruitment will include outreach to patient families seen by either the Vanderbilt Pediatric Primary Care Clinic or surrounding community practices. To improve efficiency in light of our restrictive eligibility criteria, we will use Vanderbilt’s StarPanel, a computerized electronic medical record database and Vanderbilt’s Whiteboard, a scheduling database, to generate lists with scheduled clinic dates of potential participants that meet BMI, age and zip code eligibility criteria.[50] Specifically, clinic staff will provide a list of participants to research staff that meet eligibility criteria which serves as a pre-screen to identify targeted, potentially eligible, participants and invite them into the trial. With these lists, we will also send out an invitation letter to prospective participants that includes an opportunity to opt-out recruitment efforts whereby these families that do not wish to be called or approached in clinic’s waiting room, may contact research staff to opt out of receiving any recruitment phone calls or being approached on-site at clinic ***(see appendix D for the invitation letter)***.

The Monroe Carell Jr. Children’s Hospital at Vanderbilt Division of General Pediatrics serves families from Davidson County, caring for a panel of 15,000 patients, many of whom reside in the zip codes of interest (refer to letter of support). Ninety percent of patients qualify for Medicaid. Moreover, the Cumberland Pediatric Foundation, including more than 200 community pediatricians in middle Tennessee, will refer eligible parent-child dyads to the study (refer to letter of support). The majority of children served in these clinics are 5 years old and younger presenting for well-child examinations. Utilizing this multi-pronged, recruitment strategy, we plan to reach our required numbers of study participants.

Informed Consent

Informed consent will be obtained on the same day of baseline data collection. Prior to obtaining the informed consent, adult parents and their preschool-aged child will conduct a brief eligibility screening, specifically, re-measuring height and weight to confirm the eligibility requirement of the child's BMI ***(see appendix G for script for consenting with children)***. If the child participant meets BMI eligibility criteria (≥ 50% and <95%) then the child will be escorted to an on-site child activity room, while the parent will be invited to initiate an informed consent process. Families that do not meet the eligibility criteria will receive a small token of our appreciation of their time and would not be eligible to participate for the specific cohort recruitment period; however if they become eligible for future cohort recruitment periods, they could be reassessed. Participants that do not meet eligibility criteria, data will be destroyed.

Informed consent will be obtained in a private space within a public meeting place of the community center before the initial baseline measurements. While both parents and all in the family are invited to attend sessions, only one adult (either mother or father) will be present for the consenting process and enrolled in the program, since the parent or legal guardian must be willing to commit to the 3-year study (see 11E below for eligibility criteria). During the consenting process, the child will be escorted to the childcare room located in another room at the community center.

For all consent forms, we will ask participating adults if they would prefer to use English or Spanish to understand their role in the research study. With their language of preference, informed consent forms will be handed to participating adults and then read and reviewed in the language of preference. We model our current informed consent on our recently completed study (IRB No. 100591). We include some critical questions to ask parents to ensure they understand the consent form before signing it. If the participant gives consent, they will sign and date one copy of the form and keep another for their reference; both forms are also signed and dated by the study team member obtaining the informed consent.

Inclusion Criteria

Eligibility inclusion criteria for participation in this study are as follows:

- Three-to-five year old children
- English- or Spanish-speaking
- Child's BMI ≥ 50% and <95%
- Parental commitment to participate in a three year study
- Consistent phone access
- Parent age ≥ 18 years
- Parents and children must be healthy, that is without medical conditions necessitating limited physical activity as evaluated by a pre-screen ***(see appendices E & F)***
- Child completion of baseline data collection on height and weight, two diet recall sessions, and at least 4 days of accelerometry and all willing survey items completed by the parent
- Dyad must be considered underserved which will be indicated by the parents self-reporting if they or someone in their household participate in one of these programs or services: TennCare, CoverKids, WIC, Food Stamps (SNAP), Free and Reduced Price School Lunch and Breakfast, and/or Families First (TANF)

- Residence in one of two Nashville regions: **East Nashville/Region 1 (37206, 37207, 37208, 37213, 37216, 37228)**: surrounding the East Community Center and **South Nashville/Region 2 (37013, 37204, 37210, 37211, 37217, 37220)**: surrounding the Coleman Recreation Center

For the purposes of this study we define the participating index "parent" as the legal guardian of the child who identifies that they spend the majority of time with that child at home. Other family members (e.g., grandmother, uncle/aunt, etc) may be recruited and enrolled in the program only if they have been granted legal guardianship via court order. During the consent process, legal documentation will be requested and stored for documentation purposes.

Per COPTR requirement, certain baseline data collection measures must be successfully completed prior to randomization. Once height and weight, at least two diet recall sessions, and at least four valid days of accelerometry from the child are completed, and all survey items families are willing to complete have been collected, parent-child dyads will be grouped into strata according to parent dominant language preference (English versus Spanish). After these requirements have been successfully completed, dyads within the strata will then be randomized to the intervention and control treatment groups.

Exclusion Criteria:

- Children who are <50% BMI or ≥ 95%
- Children outside the specified age range
- Families who do not speak English or Spanish
- Lack telephone contact
- Lack parental commitment to participate consistently for a three-year period
- Parents and/or children who are diagnosed with medical illnesses where regular exercise might be contraindicated
- Children who display dissenting behaviors during baseline data collection
- Parents/children who do not otherwise meet the eligibility criteria listed in section above as determined by pre-screen

Inclusion Statement: **The GROW study operationally defines participants using the following inclusion criteria:**

Child: Developmentally normal three-to-five year old children with a BMI ≥ 50% and <95%.

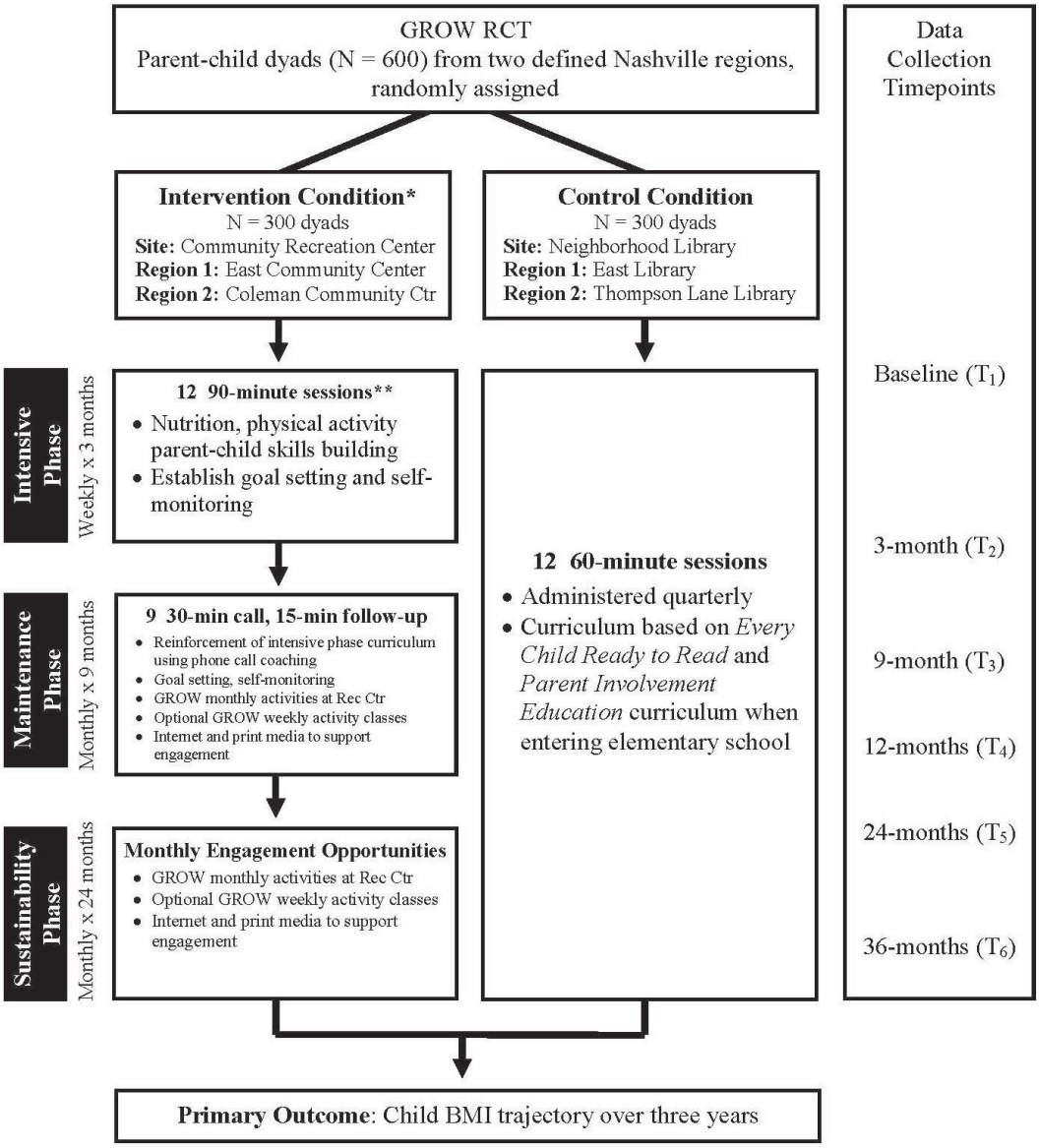
Adult: Healthy (without medical conditions necessitating limited physical activity) adults age 18 or older and designated as the child's parent or legal guardian.

Family: Speaks English or Spanish, resides in the defined vicinity of the intervention community center or control library, has a commitment to the 3-year study, has phone access, and resides in a household that participates in an assistance program for the underserved (e.g. TennCare, WIC, SNAP, free/reduced price school lunch).

Study Procedural Overview

Figure 1: GROW Trial RCT Study Phase

GROW RCT Design



*The intervention group will also receive the quarterly-administered control curriculum
**All intervention sessions will include a tested curriculum with groups of up to 17 dyads and will promote social network development

Three study waves or cohorts of participants (200 parent-child dyads each) will be invited into the study every year up to the 3rd year. In each cohort, 100 parent-child dyads will be randomized to the intervention; and 100 parent-child dyads will be randomized to the control condition. These dyads will be further broken down between two community recreational centers (intervention) and two libraries (control), subsequently 50 parent-child dyads will be participate at each site in each cohort. These 50 parent-child dyads will be further broken down and divided by their availability to attend group sessions during the week. ***See Table 1 for Study Cohorts & Timeline.*** This design: staggering intervention and control groups with 3 cohorts over a span of a 5-year time period, will allow performance sites (i.e., community

centers and public libraries) to manage the flow of study participants in addition to serving their typical number of patrons throughout the year.

Table 1: Study Cohorts & Timeline

COHORT 1		
Recruitment	May 2012	6 months
Baseline data collection	August 2012	2 months
Intervention	September 2012	36 months
Follow-up data collection	3, 9, 12, 24, and 36 months	2 months
COHORT 2	**Start**	**Duration**
Recruitment	December 2012	6 months
Baseline data collection	June 2013	2 months
Intervention	June 2013	36 months
Follow-up data collection	3, 9, 12, 24, and 36 months	2 months
COHORT 3	**Start**	**Duration**
Recruitment	September 2014	6 months
Baseline data collection	March 2014	2 months
Intervention	March 2014	36 months
Follow-up data collection	3, 9, 12, 24, and 36 months	2 months

Study Treatment Groups

The intervention group will have three phases: 1) an intensive phase (weekly for 3 months) on nutritional, physical activity and parenting skills-building via 90-min in-person sessions that promote new social networks ***(see appendix O for GROW Curriculum and refer to modules attached)***. One example of a module would be setting family goals around nutrition and physical activity. We provide encouragement to utilize the built-environment for routine family physical activity and access to healthy foods using internet/mail media, email and mail media; 2) a maintenance phase (monthly for 9 months) via 30-min phone coaching calls to reinforce concepts from phase one ***(see appendix I)*** and a brief 15-min follow-up call one week later ***(see appendix J)***, continued encouragement through internet and mail media, the availability of weekly activity programming for parent-preschool child dyads through the recreation centers, and monthly 60-minute GROW events for families to reinforce key messages; and 3) a sustainability phase (monthly for 24 months), where there is a discontinuation of phone call coaching and continuation of the other elements from phase two. The three main pillars of behavior change will be applied at each face-to-face and phone coaching session: 1) goal setting; 2) self-monitoring to achieve those goals; and 3) problem-solving. Additionally, after each measurement point in the intervention group, both the parent and child participants will receive a feedback report on growth in the form of an age-and gender-appropriate BMI curve with an explanation of how their child is growing as well as their own BMI information with an explanation.

The control condition will have only one phase: 60-minute in-person sessions delivered quarterly for 36 months, a total of 12 sessions over a period of 3-years. The core curriculum training will involve developing parental skills while also creating a practice-based learning

environment for parent-child dyads around school success utilizing key elements of *Every Child Ready to Read,*[51] a project of the Association for Library Service to Children and the Public Library Association ***(see appendix P for the Control Curriculum.*** These sessions will be led by bilingual facilitators who are trained educators that work with the Nashville Public Library Foundation. As children age in the study and enter elementary school, the control parent-child dyad will receive a curriculum that integrates core elements from the *Parent Involvement Education* curriculum, tested and implemented by the *Parent Institute for Quality Education (PIQE)* to improve school success.[52]

Data collection sessions will be conducted for both treatment groups at 6-points in time (T_1-T_6): baseline, 3-months, 9-months, 12-months, 24-months, and 36-months. Each of the six data collection points in this study will be conducted on-site at either community recreational center (i.e., Coleman and East Park) with Metro Parks staff and research staff. Metro Parks staff will not be "engaged" with research but will handle flow, childcare and check-in with participants. This data collection process will involve adult-child dyads to proceed through a variety of stations to gather measurements and information for study analysis.

Facebook use throughout the study for the Intervention Group

Since our targeted population are underserved families, such families have been well-known in the literature to be hard-to-reach and hard-to-keep families, especially over a 3 year period of time. Because of this challenge, Facebook has been considered a viable tool to retain and reach families, in addition, serve as an interactive tool to continually maintain engagement for participants in the GROW study (***see appendix H for Facebook messages).*** Thus, all study participants in the intervention groups will be invited to join a private GROW Facebook group. Specifically, through our group page, members will receive reminders to upcoming sessions/community events, polls to gauge satisfaction and curriculum understanding, posts that display recipes, pictures, and videos, and links to helpful web pages for more information. In addition, Facebook group members will be able to post comments and pictures, and hopefully strengthen their social network ties amongst themselves. This Facebook group page will not be accessible to the general Facebook community nor the community in the control condition. Per Vanderbilt Social Media Policies, research staff will monitor content daily to ensure appropriate discourse and interaction that uphold the standards of Vanderbilt as an institution. For those families that do not have a Facebook account, emails and/or regular mail will be sent out monthly.

The Adaptive Intervention Design

The research team plans to utilize an adaptive intervention approach[53] for children who are not responding to the intervention based on their BMI trajectories. More simply, for the purposes of this adaptive intervention, a child will be considered a non-responder if her/his BMI weight categorization shifts negatively from T1 to T2 (i.e., if formerly normal weight child shifts to overweight or obese in this period of time; or if formerly overweight child shifts to obese, as defined by BMI). Child BMI change from T1 to T2 will be reported using an easily understandable and comprehensive growth feedback report and mailed to the parents after T2 measurements are collected. The adaptive intervention will occur at the first phone call coaching session of the maintenance phase. The coach will review the feedback report with the parent and solicit from the parent both the successes and barriers faced with incorporating GROW lessons into their everyday lives (responders will also receive feedback reports but will not receive a report explanation session discussed by a phone call coach). These adaptive intervention report feedback sessions will occur again after BMI categorization/non-responder status is reassessed at the T3, T4, and T5 data collection time points.

Outcome Measures & Procedures

Primary Outcome

The primary outcome for this study is the child's BMI Percentile. Collected overtime through six data collection points, the change of BMI% will be used to assess the trajectory of the child's growth during the study duration. Additional anthropometric measures correlated with BMI and more specific in identifying adiposity will also be collected, such as triceps skin fold and waist circumference. Together, these measures yield a stronger indication of the rate of adiposity and the BMI trajectory overtime during a child's formative years of child development. ***See Table 2: Primary Outcomes below for details.***

Table 2: Primary Outcomes

Domain	Measurement Tool	Description	Respondent [Parent (P) or Child (C)]	Method	Collection Time
Early Childhood BMI Trajectory	Scale, stadiometer	Change in BMI% over time	C	Weight (kg)/height (m^2)	$T_1 – T_6$
Body Fat % (Triceps Skin Fold)	Caliper	Change in % body fat over time	C	Staff measured	$T_1 – T_6$
Waist Circumference	Measuring tape	Change in waist circumference	C	Staff measured	$T_1 – T_6$

Secondary Outcome

A secondary outcome of this study is parental BMI. Similar to the reasons above, additional anthropometric measures will also be included to assist in identifying a more precise measure of adiposity and BMI trajectory overtime. Since the focus of our intervention is both the child and the parent to improve health. ***See Table 3: Secondary Outcomes below for details.***

Table 3: Secondary Outcomes

Item	Measurement Tool	Description	Respondent [Parent (P) or Child (C)]	Method	Collection Time
BMI	Scale, stadiometer	Change in BMI over time	P	Weight (kg)/height (m^2)	$T_1 – T_6$
Body Fat % (Triceps Skin Fold)	Caliper	Change in % body fat over time	P	Staff measured	$T_1 – T_6$
Waist Circumference	Measuring tape	Change in waist	P	Staff measured	$T_1 – T_6$

		circumference			

Collection of Moderators & Mediators

Conceptually, moderators identify on whom and under what circumstances the study treatment have different effects. In contrast, mediators identify why and how the treatment works or doesn't work. Below is a table including all moderators and mediators identified for this study, the measurement tool, a brief description, the intended respondent, method and time point of data collection. ***See Table 4: Collection of Moderators & Mediators below for details.***

Note: Computerized surveys are electronic surveys from the REDCap Database that will be administered and completed at the community center; no procedures will be conducted at Vanderbilt nor at home. Once entered and saved, the data will be housed on a Vanderbilt server. REDCap provides the ability to enter measurement data, including basic mathematic and logic checks for verifying valid data, as well as survey data. The research staff will utilize a combination of the wireless internet at the community center and mobile hotspots to provide internet access for all computers used.

Table 4: Collection of Moderators & Mediators

Domain	Measurement Tool	Description	Respondent [Parent (P) or Child (C)]	Method	Collection Time
Physical Activity	Accelerometer (GT3X+)	Sedentary activity (% sedentary mins/total wearing time)	P, C	Parent and child accelerometer wear (≥4 days, ≥6 hrs/day)	T_1, T_2, T_4, T_6
		Self-reported physical activity habits		Computerized Survey (2Q)	
	GROW developed survey questions related to intervention messages		P		T_1 – T_6
Nutrition	Diet Recall Parent's Child's	Total calories and macronutrient content (% fat, protein, carbohydrate) adherent to USDA recommendations	P	3-day parent and child diet recall (parental report for child)	T_1, T_2, T_4, T_6

		Parent and child eating and feeding habits		Computerized Survey (8Q)	
	GROW developed survey questions related to intervention messages		P		T_1 – T_6
Social Network	GROW developed Social Network Survey	Assessing social networking and its influence on behavior modification	P	Computerized Survey (20Q)	T_1 – T_6
	Bollen & Hoyle Perceived Cohesion Scale	Assessing group cohesion Assessing information sharing	P	Computerized Survey (6Q)	T_1, Wk 4, T_6
	GROW developed Advice Scale		P	Computerized Survey (2Q)	T_1, Wk 4, T_6
Parenting Practices	Toddler Feeding Questionnaire (TFQ)	Parenting approaches to child feeding	P	Computerized Survey (31Q)	T_1 – T_6
	Child Feeding Questionnaire (CFQ)	Parenting beliefs on child feeding	P	Computerized Survey (3Q)	T_1 – T_6

Eating Together	Healthy Habits Healthy Kids (HHHK) - Eating Behaviors subscale GROW developed survey questions related to intervention messages	How often meals are eaten together Where meals are eaten together	P P	Computerized Survey (3Q) Computerized Survey (3Q)	$T_1 - T_6$ $T_1 - T_6$
Sleep	GROW developed survey questions related to intervention messages	Parent and child sleeping habits	P	Computerized Survey (6Q)*	$T_1 - T_6$
Media Use	Stanford (GEMS/ ECHALE) developed questions Youth Risk Behavior Survey (YRBS) subscale	Media available in household Child's media use	P P	Computerized Survey (3Q) Computerized Survey (3Q)	$T_1 - T_6$ $T_1 - T_6$
Use of Rec Center	GROW developed survey questions related to intervention messages	Parent and child knowledge and use of rec center outside of GROW activities	P	Computerized Survey (3Q)	$T_1 - T_6$
Perception of the Built Environment	Participant Physical Activity and Neighborhood Supports Survey	Parent knowledge of the resources in the built environment	P	Computerized Survey (40Q)	T_2
Stress	Cohen's Perceived Stress Scale (PSS)	Assesses current levels of parental stress	P	Computerized Survey (10Q)	$T_1 - T_6$

Depression*	Center for Epidemiological Studies-Depression Scale (CES-D)	Assesses levels of parental depression	P	Computerized Survey (20Q)	T_1 – T_6
Goal Setting and Monitoring	GROW developed survey questions related to intervention messages	Ability to set and track goals	P	Computerized Survey (6Q)	T_1 – T_6
Executive Functioning	Stephanie Carlson's Executive Function Scale for Preschoolers	Comprehensive executive functioning measure	C	Hands-on Tasks	T_1, T_6
Literacy	Receptive One-Word Picture Vocabulary Test, 4th edition (ROWPVT-4)	Child literacy aptitude	C	Hands-on Task	T_1, T_6
Weight Perception	COPTR common survey questions	Current perception of parent's and child's weight	P	Computerized Survey (2Q)	T_1 – T_6
Self-Efficacy	Parenting Sense of Confidence (PSOC) Scale	Confidence around parenting decisions	P	Computerized Survey (16Q)	T_1 – T_6
Demographics	GROW developed survey questions	Demographic information	P	Computerized Survey (17Q)	T_1
Genotype	Oragene kit (adult), baby brush (child)	Genetic risk score	P, C	Genotyping saliva	T_1
Perinatal Health	Updated questions from KA Dept of Health WIC intake	Maternal gestational health, birth weight, and breastfeeding habits	P	Computerized Survey (5Q)	T_1
Health Literacy	The Newest Vital Sign (NVS)	Understanding food label information	P	Computerized Survey (6Q)	T_1
Food Security	USDA 2008	Financial barriers	P	Computerized	T_1

	subscale	affecting availability of food in the home		Survey (6Q)	
Intelligence	Woodcock-Johnson III Tests of Cognitive Abilities – Brief Battery	Standard intelligence measurement	C	Hands-on Task	T_1

*****Participant will be alerted and provided appropriate resources for treatment if CES-D total score indicates severe depression (i.e., a CES-D total score of 27 or greater).

Process Measures

The GROW trial process measures will include: participation rates collected via attendance logs; data collection process collected via timed logs and identification of any issues that arise during the data collection procedures; retention barriers and facilitators via call logs conducted by the study team; session fidelity checks to ensure consistency and accuracy of content administration; logs to assess use of recreation center and library outside of mandatory GROW-related sessions; Metro Parks and Recreation facility staff satisfaction surveys to assess barriers and facilitators of conducting the research program within their facility; library facility staff satisfaction surveys to assess barriers and facilitators of conducting the research program within their facility; and parent-child satisfaction with study participation.

Description of Measures

Anthropometric Measurements

Body weight for each subject will be measured, after voiding and wearing light clothing, to the nearest 100 g on a calibrated digital scale. Body height without shoes will be measured to the nearest 0.1 cm with a stadiometer. BMI will be calculated (weight [kg]/height [m^2]), using the standard CDC calculator**.** Both height and weight measures will be collected twice. The mean of the two closest measures is used as a final measurement. Children will be wearing light clothes and without shoes. Height without shoes will be measured to the nearest 0.1 cm using our standard stadiometer (Perspective Enterprises, Portage, MI). Adult and child waist circumference will be measured with a fiberglass measuring tape on the skin, at the umbilicus, to the nearest 0.1 cm, according to the recommendations of the World Heart Federation.[54] Waist circumference will be collected two times, if the two measurements of waist differ by 1 cm or more, then the waist measurements are repeated a third time and data entered. The mean of the two closest measures is used as a final measurement. Measurements will be obtained by trained project staff and standardized according to accepted standards.[55-57]

Triceps Skinfolds

Triceps skinfold thickness is a measure of subcutaneous fat and is a component of equations used to predict body fat composition.[58] SFs have been used successfully in studies with adults and children,[59-61] including young children from 3 to 8 years of age.[62,63] Recent literature suggests that SFs are more accurate in estimating body composition compared to bioelectrical impedence (BIA) during the adiposity rebound, the normal pattern of growth that occurs in all children growing between 3 to 5 years of age.[62] SF is measured using a 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 project of the acromion process of the scapula (shoulder blade) and the inferior margin (bottom) of the olecranon process of the ulna (elbow). They are measured to the nearest 0.1 mm and collected two times. A third SF measurement is taken if either of the following occur: 1) If the two triceps values are less than 10mm but differ by 2 mm or more; or 2) If the skinfold is 10mm or larger, with a difference between the two measurements of greater than 10% (((maximum-minimum)/minimum)*100). In either case, the mean of the two closest measures is used as the final measurement. In order to accommodate participants that are morbidly obese participants then we will use the Harpenden calipers. Training, certification and quality control procedures for SFs are similar to those outlined above for waist circumference and other anthropometrics.

Accelerometers

Amount of physical activity will be assessed using the ActiGraph GT3M (Actigraph LLC, Ford Walton, FL) accelerometer. Accelerometry had been used successfully in studies with adults and children[64-68] with a reliability: r = 0.93 [69] . Both a parent and a child will be asked to wear the monitor for one week during waking and sleeping hours except when bathing, showering, or swimming. A simple 1-page manual (in Spanish and English) will be provided. The monitor will be attached to a belt secured at the waist. The monitors will be sent by mail in pre-addressed and pre-stamped boxes to the Energy Balance Laboratory at Vanderbilt. We have used this technique very successfully in similar studies with children and their families. The activity data will be downloaded to a computer and analyzed. Physical activity will be expressed as activity counts per day. Total and physical activity energy expenditure (kcal/day) will be calculated using validated equations.[69,70] Threshold values from a validation study will be used to calculate time spent in sedentary, light, moderate, and vigorous activity. Accelerometer use will be supplemented with a short physical activity log that collects physical activities and time of accelerometer use (hours/day).

Energy Intake

We will obtain detailed data on foods and nutrients associated with energy balance and weight management from total dietary intakes (foods, beverages and snacks): energy intakes, energy density, macronutrient intakes, added sugars, as well as consumption of specific foods and food groups that are excessively high (Sugary Sweetened Beverages, desserts) or inadequate (fruits, vegetables, milk and dairy products, whole grains and fiber) in the typical diets of U.S. children. It is understood that accurate assessment of dietary intakes of free-living individuals is a challenging process and there is no single method that is without limitations. To optimize the accuracy of the assessment of dietary intake data, we will conduct 24-hour dietary recalls using the USDA multi-pass method administered by trained diet recall technicians. Recalls will be performed to capture the average of dietary intakes from 2 nonconsecutive week days and 1 weekend day during the 14-day period of each main study time-point. Diet recall will occur via three phone sessions conducted by the two master trainers at the University of North Carolina (UNC) at Chapel Hill over a maximum of a 30-day period to collect complete participant information. All master trainers will participate in a central in-person training organized by the Research Coordinating Unit (RCU) located at UNC. No diet recalls will be conducted until after the trainer has been trained and certified. Parents will report on themselves and on their child. Analyses will not include data that indicates unrealistically low (eg, <600kcal/d) or high intakes

(eg, >4000kcal/d). Dietary data will be entered and analyzed using our NDS-R software (Nutrient Data System for Research, St. Paul, MN). Added sugars will be calculated using the USDA database (http://www.ars.usda.gov/Services/docs.htm?docid=12107)

Study Questionnaire

The study questionnaire will measure a variety of domains and will be provided in both English and Spanish ***(see appendix K for survey)***. It will be a computer-administered questionnaire competed by parents with paper and pencil questionnaire as back-up. ***See Table 4: Collection of Moderators & Mediators above for details***. Survey takes about 30-45 minutes to complete.

Social Networks

We will collect social network data, exploring the potential development of new social ties that could result due to the structure of the study ***(see appendix L).***

Genetics

Saliva will be collected from the parent-child dyad participating in the study[71]. For adults, saliva will be obtained utilizing the Oragene saliva kit, collecting 2-3 cc of saliva per participant. For young children, saliva will be obtained utilizing the "baby brush" approach, in which small sponges attached to plastic handles are inserted between cheek and gumline to absorb saliva. Subsequently, the sponges (x4) are cut and placed in the spittoon with DNA preservation solution. We will then use a modification of the Puregene DNA (Gentra, Inc) Purification Protocol for 4 ml Saliva Samples[71], consisting of 4 stages: (1) cell lysis and adddition of RNase to remove RNA from the salivary nucleic acid; (2) DNA precipitation in 100% isopropanol, with 70% ethanol wash; (3) DNA hydration in reduced TE (Tris EDTA) to approximate concentration of 200 ng/u; (4) DNA storage at 4C for working stock, and -80C for archival DNA samples.

Barriers to Physical Activity Questionnaire

This study survey is based from the *Environmental Supports for Physical Activity Questionnaire*[72] to assess individual perceptions of physical activity supports in the social and physical environment, use of the built environment, current physical activity behavior and recreation center use. This survey will take about 15-20 minutes to complete and has been validated in previous literature.[73] These data will help describe the policy environment of study participants and identify policies that enable or constrain active living for participants. The objective of this survey is to link current behavior with local community policies. Specifically, to determine specific neighborhood characteristics that enable or constrain participant ability to be physically active, match participant responses to one of the three policy types: personal safety, transportation, and land use, describe local and state policies that address participant responses, and identify untapped policy options for improving physical activity levels in participant communities.

Control Measures

The study will use Stephanie Carlson's Executive Function Scale for Preschoolers to determine a comprehensive measure of executive functioning in the child participants of the study. The battery of hands-on tasks (e.g. card sorting) will be administered by a trained data collector one-on-one to each child and is estimated to take approximately 10 minutes. To measure

intelligence of the child participants, the research team will use the Woodcock-Johnson III Tests of Cognitive Abilities – Brief Battery. This tool involves a battery of tasks where children expressively (verbally and/or through pointing) respond to an assortment of pictures and words in a flipbook. Trained data collectors will administer this test individually with each child. The brief battery is estimated to take between 15 and 20 minutes to administer.

Incentives

Data Collection Incentives

After each data collection session, participating families will receive gift cards of varying amounts throughout the duration of the 3-year trial (See Table 5 below for details). At times 1, 2, and 4 participants will receive $40. At times 3 and 5 participants will receive $15 gift card. One the final data collection time, participants will receive $50. Please see the table for additional information.

Table 5: Data Collection Incentives

Data Collection Point	Amount	When
T1 (Baseline)	$40.00*	At randomization
T2	$40.00*	Pick up day
T3	$15.00	Immediately after
T4	$40.00*	Pick up day
T5	$15.00	Immediately after
T6	$50.00*	Pick up day

*Participants will receive half of the incentive upfront prior to wearing accelerometers and the other half upon return and completion of at least 2 of the 3 diet recalls.

Intervention Incentives

Intensive Phase: Participants will receive tangible tools or small giveaways during each session. The value of these items will be approximately $3.50 per parent and child dyad each week when sessions occur. Examples of tangible tools, items to reinforce lessons learned are kitchen ware utensils, measuring spoons, etc. In addition to the tangible tools, in order to encourage attendance during the intensive phase of the intervention (weekly for 3-months), participants will have an opportunity to enter a raffle. These raffles will be held during sessions 3, 6, 9, and 12 (see table 6 below for details). The odds of winning the raffle in the intervention group is about 1:15, assuming that on average there are 15 people in attendance each week. Notably, the odds vary based on the number of sessions each person attends individually and the number of attendees in the session. Moreover, there will be a separate raffle for each intervention group for each cohort. Specifically, there will be between 6-8 intervention groups per cohort (3-4 groups per site). If participants attend all 12-sessions during the 3-month intensive phase, participants will receive a value amounted of $42 worth of small gifts.

Table 6: Data Collection Intervention Incentives

RAFFLE	ITEM*	VALUE
Session 3	Hand mixer	$10.00
Session 6	Food storage containers	$15.00

Session 9	Mixing bowls	$20.00
Session 12	Casserole dish	$25.00
TOTAL		$70.00

*We may substitute items of similar value
Note: These items were based on a kitchen inventory administered by our nutrition team. 42-57% of those surveyed did not have these items.

Maintenance Phase: Participants will receive a coupon for a free fitness class of their choice valid at either community center location each month that coaching calls are completed (monthly for 9-months). Fitness classes such as zumba, line dancing, or yoga, etc are routine services offered to the general public at each of the community recreational centers. The value of this coupon is $2.00. Participants that complete all 9-monthly phone coaching calls during the maintenance phase will receive a value of $18 worth of fitness classes for 9-months.

Maintenance and Sustainability Phase: Participants will be invited to participate in classes and various community center events throughout the duration of the maintenance and sustainability phases. Apart from the fitness classes, which are offered by the community centers, we will offer GROW-related community events that focus on nutrition and/or physical activity with parents and children once per month throughout the duration of the 3-year trial. For each class or event attended, participants will receive one punch on their punch card. After every 6 punches, participants will redeem the punch card for a gift valued at $5.00. These small gifts will include kitchen gadgets such as an apple corer, spatula set, wooden spoon set, etc. If participants attended every event during the 3-year trial, participants will have 5 opportunities for a gift valued at $5.00, resulting in a total amount of $25 worth of small gifts in 33-months (maintenance and sustainability phases).

Control Incentives

Similar to the intensive phase of the intervention incentives, all participants will receive tangible tools or a small giveaway during each session. The value of these items will be approximately $5.0 per parent and child dyad when sessions occur. Examples of these giveaways are books, etc. If participants attended all sessions for 36-months, participants will receive a value of $60 worth of small gifts. In addition, at every session, all attendees will be entered in a raffle to win a $20.00 gift card (quarterly for 36-months). Similar to the intervention group, the odds of winning the raffle in the control group is about 1:15, assuming that on average there are 15 people in attendance.

For both intervention and control groups, these additional incentives should not pose or be considered coercive since families had already consented to participate in the study. All incentives are tied specifically to participation within the trial and were recommended by families in our prior work in the GROW Formative Phase (IRB No: 100591).

Health-related Incentives

In addition to these incentives, all participants from both intervention and control groups in the study will receive family memberships to their respective community recreational center for one year, which allow adults to use the weight room for no cost, and families to take swimming lessons at 50% of the normal cost. These family memberships will be given to all intervention families during the study and all control families at the end of the study. Moreover, if families use the facility at least once per month, then their family membership will be extended year by year

up to 3-years. This will encourage families to utilize their built environment for family physical activity.

The value of the parent and child gym membership for one year equates to $400 at each community center. Although this may be interpreted as undue inducement for families to participate in a 3-year RCT study, providing gym membership to participants allows increased physical activity and healthy living - a direct benefit and positive health advantage to subject participants and their families as opposed to compensation of monetary or economic gains. Since increasing physical activity is directly related to the outcome of the study, we conceptualize offering gym memberships as a bonus and a justified benefit for those that have participated.

Randomization

Randomization Schedule

An identical randomization procedure will be followed for each of the three successive cohorts. Available software (e.g., SAS, Stata) will be used to generate a blocked randomization schedule per each strata, within both regions, resulting in 4 total schedules (2 language conditions x 2 regions = 4). Block size will be randomly permuted with the software procedure (although no larger than 10), thereby insuring equal representation at intermittent recruitment points while minimizing the probability of correctly guessing subsequent condition assignment.

Each schedule will be identified by stratum and loaded into the recruitment database. The database security settings will be specified so that once loaded no one on the study team will have write privileges for the schedules, and only the statistician will have read privileges. These settings will prevent anticipation (except for the statistician) or subversion of the randomization process by any member of the study team.

Random Assignment

Each potential dyad's contact information, including child age and dominant language use, will be loaded into the recruitment database upon identification as a potential participant and assigned a unique study identification number (family id). The recruitment database will follow each potential dyad from the point of identification through eligibility assessment and enrollment through disqualification or randomization. The recruitment database will track all eligibility and enrollment criteria and include a utility that checks still-eligible study candidates for criteria that must be met prior to randomization. Upon identifying dyads who have met all of these criteria, recruitment staff will engage a database utility that performs randomization by identifying the stratum into which each potential dyad should be randomized, and populating the next available slot in the appropriate randomization schedule with the dyad's family id. The database user will not be able to see, and will be unlikely to anticipate, the arm assignment (treatment versus control) for each dyad, especially when multiple dyads within a stratum are randomized at once. Once the dyad is assigned to an arm, a link is established between family id and arm assignment (treatment versus control). This link will not be writable by any study staff and will be viewable by the study statistician in the randomization schedules. Dyad's assignments will be viewable by all study staff on a case by case basis so that the daily activities of managing participants, both parents and their children, may be done without hindrance.

Randomization Data Management

The link between family id and arm assignment will be stored in the randomization schedule, to which only the statistician will have read access. All randomized dyads will remain in the recruitment database for the duration of the study so that recruitment and enrollment reports can be generated on demand by all study staff. By viewing a dyad's record, any study staff can view but not edit the dyad's arm assignment.

All dyads' family ids will be exported into a measurement database along with the fields necessary to conduct timely data collection and on-demand reporting by any study staff. Arm assignment will not be exported to the measurement database. As such, it will not be possible for measurement staff to know a dyads's arm assignment based on the information available in the measurement database.

In addition, once randomized, the family ids (both treatment and control) will be exported into an intervention database along with the fields necessary to conduct the treatment and control procedures and allow on-demand reporting. Arm assignment will not be exported to the intervention database, although its value is implicitly known. As such, intervention staff (in both the control and treatment conditions) will know which dyads have been assigned to which arm, but this knowledge is unavoidable and redundant with knowledge that will be apparent from contact with the dyads within each arm.

Randomization Data Safety

All databases (recruitment, measurement, etc.), will be stored within a password protected shared drive within the university computer system. All study staff will have access to the databases upon submitting the required password. Access to tables within these databases will be made available as needed to perform job responsibilities and in accordance with COPTR policies. The randomization schedule will not be stored in the intervention database making it impossible to access in this manner.

Risk/Benefit Analysis

There are minimal research related risks associated with this study. For this study, suggested exercises will be mild and are unlikely to cause injury. All suggested dietary changes are evidence-based and healthy. If any physical injury or illness should occur as a direct result of participation in this study, VUMC maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. The informed consent document will include this statement and will provide pertinent contact information.

The risks to subjects of the study are reasonable, given their minimal nature (e.g., suggested low-moderate physical activity options and healthy dietary changes; learning how to engage their children in dialogue) and given the safeguards employed, as described above. In contrast, we expect tangible benefits to accrue to all subjects of the study: intervention group participants are expected to experience improved healthy lifestyle habits and health outcomes as a result of participating in the study; control group parents are expected to experience empowerment in their ability to prepare their child for school and control group children are expected to be better prepared for school as a result of participating in the study. Also all participants are expected to experience increased parent-child bonding as a result of participating in the study. All participants in the will receive family memberships to their respective community recreational

center, depending on which treatment group will be during or after study implementation, which allow adults to use the weight room for no cost, and families to take swimming lessons at 50% of the normal cost.

Data and Safety Monitoring Plan

General Description

Comprehensive measures will be implemented to maintain subject confidentiality as appropriate. Study ID number will identify all data collection materials for the study. Only study team members will have access to master linkup lists that match participant names to these Study ID numbers.The master link-up list linking names and Study ID numbers will also contain some basic demographics to be collected for purposes of the study (e.g., gender, maternal education) and personal health information (weight, height, body composition). All data collection forms will be housed at VUMC.

All study data will be kept at VUMC securely locked in a storage area for this study. All data will be obtained specifically for research purposes. The study investigators reviewing the data will not be provided with any participant identification information. Study data collection forms will be maintained under lock and key for 10 years following completion of the study. Thereafter, they will be destroyed. All electronic data files will be stored on a password protected, secure, encrypted server. Only key study personnel will have access to the password. Ten years after study completion, electronic copies of all datasets will be destroyed. Individuals will not be identified in any publications of the study findings.

Data Safety and Monitoring Plan

Purpose: The Data and Safety Monitoring Plan is written to ensure the safety of the participants and to verify the validity and integrity of the data.

Assessment: Participants will be assessed for adverse events at the time of enrollment and when the data is collected at each time-point. The Principal Investigator, co-investigators, study coordinator, intervention lists and all members of the research staff are responsible for the assessment and reporting of adverse events. All spontaneous reports by subjects, observations by clinical research staff, and reports to research staff by family or health care providers will be investigated. The investigators will assess the relationship of the adverse event as not related, possibly related or definitely related using standard criteria for clinical trials.

Possible (to qualify, the adverse event must meet 2 of the following conditions):

1) has a reasonable temporal relationship to the intervention,
2) could not readily have been produced by the subject's clinical state,
3) could not readily have been due to environmental or other interventions,
4) follows a known pattern of response to intervention,
5) disappears or decreases with reduction in cessation of intervention.

Probable (to qualify, the adverse event must meet 3 of the following conditions):

1) has a reasonable temporal relationship to the intervention,
2) could not readily have been produced by the subject's clinical state,
3) could not readily have been due to environmental or other interventions,
4) follows a known pattern of response to intervention,
5) disappears or decreases with reduction in cessation of intervention.

Definite (to qualify, the adverse event must meet at least 4 of the following conditions):

1) has a reasonable temporal relationship to the intervention,
2) could not readily have been produced by the subject's clinical state,
3) could not readily have been due to environmental or other interventions,
4) follows a known pattern of response to intervention,
5) disappears or decreases with reduction in cessation of intervention.

Policy for Blinding in COPTR

January 26, 2012

Introduction

In all clinical trials, the potential for bias is one of the main concerns. Bias arises from conscious or subconscious factors, and can occur from the initial design through study conduct, data management, data analysis and interpretation. A general approach to avoid biases is to keep the participants and the investigators blinded to the identity of the assigned arms until all data points are collected. As stated by Friedman, Furberg and DeMets, a fundamental point is that: "*A clinical trial should, ideally, have a double-blind design in order to avoid potential problems of bias during data collection and assessment. In studies where such a design is impossible, other measures to reduce potential bias are advocated*."

Guiding principle #1: All COPTR personnel that are in a position to change the study protocol or its implementation in study participants, should be blinded to information that may allow them to do so, from when the study starts until the study ends, with specific exceptions as delineated in this document.

Clarification of terms:

- The "study starts" at a site when the first participant is randomized.
- The "study ends" at a site when the outcomes (primary and secondary) of importance to the site have been collected on all participants.
- "Interim' information is information that is collected between the study start and the study end at a given site.

As stated in the "Decision Making Protocol," there are Common and Site-specific elements:

- **Common elements** refer to those measures that two or more sites collect, protocols and manual of procedures related to those measures, and reporting processes.
- **Site-specific elements** refer to those measures and operational activities that relate to only one site.

With respect to study information/data, the following is to clarify terms:

- Study data – any information collected on study participants, which includes
  - Primary and secondary outcome variables
  - Demographic variables
  - Mediators and moderators
- Outcome variables – primary and secondary outcomes as described in site protocols
- Process variables – e.g. training, recruitment, intervention implementation, fidelity, adherence, retention/attrition

Also, data are available at multiple levels:

- Individual subject level, including subject's family or community
- Aggregated by arm, that is, collapsed from individual subject level and combined or averaged by study arm

Guiding principle #2: All COPTR study site personnel (staff and investigators) should be blinded to study data aggregated by study arm that have the potential to impact the study's outcome, or if not possible, measures need to be taken to reduce potential bias. Specific exceptions are delineated in this document.

Study data 'that have the potential to impact the study's outcome include aggregated: arm-level outcome variables, mediators, moderators (OMM), and process variables. Individual level outcome variables, mediators, moderators, process, and demographic variables are not blinded. Arm-level demographic variables are not blinded.

There may be specific process data collected in one or more arms that the Principal Investigator and study staff want to review aggregated by arm before the end of the study. Those variables will be declared *a priori* by each site, reviewed by the Design and Analysis Working Group, and approved by the PI. Those variables will be clearly listed as unblinded variables in the final study protocol. Should sites wish to examine additional blinded process variables aggregated by arm, after the study has begun, those requests would also be reviewed by the Design and Analysis Working group and, if access is approved by the PI and by the DSMB, those variables will be clearly listed as unblinded variables in an amendment to the study protocol. Subsequent references in this document to process data will distinguish between blinded and unblinded process variables.

In clinical trials that require **interim** monitoring, it is an accepted principle that interim OMM and blinded process data aggregated by arm should be kept confidential, with such data accessible only to a small number of individuals responsible for its analysis and monitoring. Generally, blinding to intervention arms should be maintained to the extent possible until the study ends. In COPTR, study investigators and sponsors are not privy to interim OMM and blinded process data aggregated by arm, and only the study or independent statisticians/analysts preparing and presenting the analysis to the DSMB, as well as the DSMB, are unblinded.

The study arms in the 4 trials are, BY DESIGN, not able to be totally blinded. However, some blinding can be maintained. Measurement staff should not be informed of the intervention that individual participants are receiving, and should have **no role** in the delivery of the intervention. Efforts should be made to avoid participant (child/parents) interactions that result in open chatting with assessors about the interventions they have received. Measurement staff should be trained to end any such communication when initiated by participants.

Study investigators and staff are kept blinded as to the ARM level results until study end. That is, they should **never** see or hear OMM and blinded process data aggregated by arms until the DSMB allows it. Exceptions to this policy are made only for individuals and circumstances in which unblinding is necessary for the preparation of reports to the DSMB. Ancillary studies need to adhere to these same principles.

Table 7. Summary of issues related to maintaining objectivity as applied to COPTR

	COPTR
Interventions are comparable and suitable for blinding	**NO, BY DESIGN**
Investigators/staff are blinded as to arm of an **individual** participant	**NOT POSSIBLE**
Individual child and/or parent participants are blinded as to the intervention they are receiving	**NOT POSSIBLE**
Outcome assessors are blinded as to the intervention the **individual** participant is receiving	**YES**
Site investigators and all study staff, except site statisticians/analysts, are blinded as to ALL the aggregated by arm interim OMM and blinded process data	**YES**
Site Statisticians/analysts at each field site are blinded as to the aggregated by arm interim OMM data on **common** measures	**YES**
Site Statisticians/analysts at each field site are blinded as to the aggregated by arm interim OMM on **site-specific** measures	**NO**
Site staff are unblinded to the aggregated by arm process measures identified *a priori* or by amendment to the protocol as unblinded	**YES**

Guiding principle #3: In COPTR, the RCU will function as the 'Independent Statistician,' while the individual study center statisticians/analysts will function as the 'Site Statistician.'

The rationale for keeping investigators and sponsors blinded to interim data is generally accepted. The possible conflict of interest that could arise for the site statistician or analyst who performs the analysis of the interim data and presents it to a data monitoring committee has received little attention. Ellenberg and George (2004) describe some potential conflicts for the Site Statistician, and approaches that might be taken to minimize them.

Ellenberg & George (2004) argue that a reason for not blinding the Site Statistician is the assumption that the Site Statistician is someone "with no obvious intellectual conflicts of interest who, by training and temperament, can be trusted to provide a dispassionate analysis of the accumulating data." This objectivity assumption may or may not be true, and there are many pressures exerted on the Site Statistician that is employed and part of the team at a study site.

Each of the 4 COPTR sites has identified an individual(s) who will serve as the Site Statistician. The **Site Statistician is the person(s) responsible and accountable** for maintaining the blind of any site-specific study OMM and blinded process data from all other site study investigators and staff. It is the responsibility of the site Principal Investigator to ensure that the Site

Statistician understands his/her role and responsibilities. The Site Statistician must have no communication with others at the site, formally or informally, about trends in OMM and blinded process data and side effects. They must also safeguard data files, printed output, log files and any emails or correspondence related to the OMM and blinded process data and side effects with the RCU and the DSMB. It is their responsibility to take care in destroying printouts and correspondence – ideally by shredding. It is also their responsibility to make sure that any discussion and communications of blinded data with the RCU and DSMB are confidential.

The Site Statistician:

i. will be blinded to aggregate comparisons by arm of post-randomization COMMON OMM data until all endpoint data have been collected at their site unless otherwise instructed by the DSMB.
ii. will remain objective when carrying out the activities of conducting the trials – preparing randomization schemes, randomizing individual subjects, processing of the data, cleaning and editing the data, preparation of analyses/reports of site-specific OMM and blinded process data, and transmitting the COMMON OMM data to the RCU; and
iii. is responsible and accountable for maintaining the blind of study site investigators and staff at their site with respect to OMM and blinded process data aggregated by arm.

The RCU:

i. is the only entity that has personnel that are unblinded to the COMMON OMM data aggregated by arm during the trial;
ii. will prepare analyses/reports to the DSMB of the COMMON OMM data and adverse events aggregated by arm, as requested by the DSMB;
iii. shares responsibility for maintaining the blind of study site investigators and staff; and
iv. is responsible and accountable for maintaining the blind of co-investigators from NIH and RCU staff who do not need to be unblinded with respect to COMMON OMM data aggregated by arm in order to complete their duties.

Responsibilities of the Site Statistician and the RCU

It is imperative that professional ethical conduct guidelines be followed by the Site Statistician and the RCU Independent Statisticians at each stage of the study. The Site Statistician prepares the randomization scheme and thus handles the list (datafile, database table, etc.) linking study ID to assignment that permits looking at the data aggregated by arm. Thus, this person(s) must exercise care in protecting the treatment allocation list and ensuring no one – including him/herself - conducts any analyses of COMMON OMM variables, adverse event or other follow-up information aggregated by arm. The Site Statistician may prepare descriptive reports of site-specific data aggregated by study arm if so directed by the DSMB or RCU. All study data must be protected in secure, password protected files or databases with only the Site Statistician, their programming staff, and the RCU having access to the data files. Note that data needed to interact with and track families (e.g., names, ages, contact info, etc), will not be blinded to interventionists, of course.

The list (datafile, database table, etc.) created by the Site Statistician that contains the subject ID and the allocation to study arm is protected in a secure and password protected manner with only the Site Statistician and the RCU having access to the information.

Blinding of Investigators by Data Type

All data collected will be categorized *a priori* into one of 7 categories:

i. *Demographic* information, such as age, sex, country of origin, and contact information is not blinded, either at the individual level or aggregated by arm.
ii. *Study arm assignment* is concealed until the time of randomization.
iii. Post-randomization, all field center or site personnel are blinded to *common OMM data, aggregated by arm*, except as allowed by the DSMB.
iv. Post-randomization, all site personnel except the site statisticians/analyst are blinded to site-specific OMM data, aggregated by arm. The site-specific OMM data, aggregated by arm, are held strictly confidential by the Site Statistician, programmers they designate, and the RCU as detailed in this document.
v. *Post-randomization, individual level process data* are viewed by the Principal Investigators throughout the study and may also be shared with the interventionists, Project Coordinator or Manager. *Arm-level process data* may be viewed by the Principal Investigators and shared with the interventionists, Project Coordinator or Manager, if those variables are first reviewed by the Design and Analysis Working Group, approved for access by the PI, and listed *a priori* as unblinded variables in the study protocol or as an amendment to the study protocol.
vi. Post-randomization, blinded process data, aggregated by arm, are held strictly confidential by the Site Statistician, programmers they designate, and the RCU as detailed in this document.
vii. *Safety data* are collected for the purpose of insuring participant safety. Guidelines for viewing these data have been designed by the COPTR Subcommittee on Recruitment, Retention, Consent, Adverse Events and Safety.

Blinding of Investigators to Study Data by Study Stage

i. **All** *baseline data* from an individual subject are collected prior to allocation to a study arm. Following all baseline data collection on an individual subject, allocation information on that subject is made available to site study staff as needed. Comparative baseline (pre-randomization) data may be viewed by investigators and study staff in aggregate by arm (e.g., for reporting comparability of groups in a design and/or baseline manuscripts). The site investigators may analyze and publish data collected at baseline using the usual policies of subject confidentiality and protection and guidelines set by the COPTR Subcommittee on Publications, Presentations and Ancillary Studies.
ii. *Interim Data (post-randomization)*. All site personnel are blinded to *common OMM data, aggregated by arm*, except as allowed by the DSMB. All site personnel except the site statisticians/analyst are blinded to site-specific OMM data, aggregated by arm. The site-specific OMM data, aggregated by arm, are held strictly confidential by the Site Statistician, programmers they designate, and the RCU as detailed in this document. *Individual level process data* are viewed by the Principal Investigators throughout the study and may also be shared with the interventionists, Project Coordinator or Manager. *Arm-level process data* may be viewed by the Principal Investigators and shared with the interventionists, Project Coordinator or Manager, if

those variables are first reviewed by the Design and Analysis Working Group, approved for access by the PI, and listed *a priori* as unblinded variables in the study protocol or as an amendment to the study protocol. Blinded process data, aggregated by arm, are held strictly confidential by the Site Statistician, programmers they designate, and the RCU as detailed in this document. **No interim OMM or blinded process data from any arm are available for publication or presentation until the end of the study, unless the plan has been (1) reviewed by the Design and Analysis Working Group and the Publications Subcommittee and (2) approved by the site PI, the Steering Committee, and the DSMB.**

iii. *Final data. Final data* are held private at each site or at the RCU in the same manner as the Interim data until the end of the study. The end of the study at each site is defined as the moment that the last study data point at that site has been collected and recorded. This includes data from all study index children as well as data from other individuals and entities at a study site. At the end of the study, all study data, including data on study arm assignment, can be accessed by study investigators using the usual policies of subject confidentiality and protection and guidelines set by the COPTR Subcommittee on Publications, Presentations and Ancillary Studies.

Preparation of Study Data Reports for the DSMB

i. Accumulated data will be 'frozen' at a specified date for the particular report. A copy of the 'frozen raw datafile of COMMON measures' is sent to the RCU for analysis along with the protected list of the treatment allocation.

ii. After processing, cleaning, editing, creating derived variables, the dated 'analysis files' of COMMON variables (including treatment allocation) and relevant documentation are sent to the RCU. Site-specific data are not sent to the RCU.

iii. For COMMON variables, the Site Statistician conducts analyses for the purposes of data cleaning and looking for outliers, unusual trends and distributional anomalies of the data from their own site, overall – **not** by study arm. They do not generate comparative analyses by study arm. Information generated (not the raw data) may be shared with other site investigator/s for the purposes of conducting data cleaning. The cleaned COMMON variables data are sent to the RCU, along with means and frequencies for all variables. The RCU will prepare means and frequencies for all variables and compare them to the site results to confirm accurate transfer of data. The RCU will prepare descriptive and quality control tables for presentation to the DSMB, both overall and by study arm. No modeling is done by the RCU unless they are specifically instructed to do so by the DSMB.

iv. For **site-specific** data, the Site Statistician conducts analyses for the purposes of data cleaning and looking for outliers, unusual trends and distributional anomalies from their own site, in a manner similar to that described above for COMMON variables. Different from common variables, the Site Statistician prepares descriptive and qualitative data reports using templates developed in cooperation with the RCU. These reports will not be generated by study arm unless instructed to do so by the DSMB. Otherwise, site-specific variables will be examined only with data from all study arms combined.

Data on Participant Safety

As with other data, safety data will be blinded, as possible, to the investigators and staff at each site (not possible when obviously related to the intervention or collected during an intervention activity, for example). The objectively collected adverse events data, however, are collected the same way in all arms and will be blinded. Sites should see only aggregate data (all treatment arms combined) although RCU can prepare data for DSMB by arms.

Treatment condition unblinding recommendations

Study arms

Decisions to unblind the site investigators to arm-level experimental assignment will be the responsibility of the DSMB according to the following steps.

i. RCU prepares adverse events and safety reports by unidentified arm (e.g., group A, group B) in the twice-yearly DSMB reports.
ii. DSMB reviews adverse events and other safety-relevant data at their periodic meetings.
iii. If the DSMB identifies a potentially important difference between arms in adverse events or other safety-related data, they may request additional analyses and/or request unblinding of arm assignment (e.g, treatment and control), and may consult with the NIH, RCU and PI(s) to help them interpret the findings. Unblinding, if necessary, should be limited to only those investigators who need to know to protect the safety of participants.
iv. If the DSMB determines that the differential between arms may impact the safety of participants and/or changes the assessment of risk of participation, they will make the appropriate recommendation to the NIH who, in turn, will notify the site PIs, accordingly.
v. It is the responsibility of the site PIs to report to their site IRBs.

Presentation of Reports to the DSMB

The RCU statisticians will be presenting the report, which includes the report on the common measures, plus each site's site-specific variables report. The Site Statisticians are available to be contacted by phone during the DSMB meeting in case questions arise that they are in a better position to answer about the site-specific variables and the overall site analyses. Site Statisticians may not participate in any portion of the meeting or call in which unblinded common OMM data are discussed.

Timeline for preparation of reports to the DSMB

Typically there is a roughly a 7-week period prior to the date of the meeting for preparing the DSMB report. Adherence to this timeline assumes that data entry and cleaning have been ongoing and that templates used to generate tables have already been created. It also recognizes that some data, such as blood analyses, actigraph, and diet data, that undergo other processing, may be delayed in comparison to other types of data.

Table 8. Timeline for preparation of reports to the DSMB

-7 weeks	• data 'frozen' for the report on same date at each field site • copy of raw frozen COMMON measures files sent to RCU
-5 weeks	• data processing, data cleaning, data editing, datafile creation at each field site completed • clean COMMON measures files sent to RCU

-3 weeks	• data reports on site-specific variables prepared, reviewed at each field site and sent to RCU • data reports on COMMON variables prepared and reviewed internally at the RCU
-2 weeks	• RCU compiles reports, assembles binders and sends to DSMB
0 weeks	• DSMB meeting

At the meeting, the RCU presents the report, and afterwards collects all reports for archival. The RCU communicates with site investigators and Site Statisticians on relevant issues raised by the DSMB – such communication is not shared with other site staff or investigators.

Communication of the Policy for Blinding in COPTR

In order to insure that this policy is clearly understood and communicated, all COPTR study Principal Investigators, the NIH Project officer, the Site Statistician and the RCU members involved in data management or analysis will confirm compliance. Over the course of the study as new personnel are hired, they will also confirm compliance. This will be done by each of these individuals sending an email to the COPTR Communications Manager as follows:

> I have read, understood and agree to comply with the 9 page document entitled, *Policy for Blinding in COPTR.*

The RCU will maintain a list of the names of individuals from whom this confirmation has been received, and this list will be available for inspection by the DSMB.

References

1. Ellenberg SS, George SL (2004) Should statisticians reporting to data monitoring committees be independent of the trial sponsor and leadership? *Statistics in Medicine* 23:1503–1505.
2. Friedman LM, Furberg CD, DeMets DL (2010) Fundamentals of Clinical Trials, 4th ed., Springer, NY.

Study Design, Statistical Consideration and Analysis Plan

Study Design

The design of the study is a longitudinal non-blinded (open) randomized control trial, comparing participants in an obesity prevention treatment program to those in a non-specific literacy-based educational control group. The trial will take place over six years. The trial will be conducted at two separate sites (region One, East Nashville, and region Two, South Nashville). Within each site, parent-child dyads with children ages 3-5 years will be randomly assigned, stratified according to parent language use (English or Spanish), to either the three-year prevention program or the control condition, yielding 600 dyads per cohort (300 per region/site), and a total

sample size of 600. Assessments will occur over six time points within each cohort, beginning at baseline and including assessments post-intervention (at 12 weeks/3 months), and at 9, 12, and 36 months from baseline.

Primary Research Question and Hypothesis

Our primary research question is about the impact of the GROW trial on the growth rate of children's BMI over time. Specifically, we hypothesize the following:

Hypothesis 1: The BMI trajectories of children in the treatment group will accelerate at a slower rate than those in the control group over time.

Primary Outcome

Although childhood obesity is a well-documented public health concern, most studies have assessed the obesity outcome (e.g., BMI) using only a single time point or incorporating a pre-post design, leaving us with little knowledge about the actual shape or growth rate of trajectories of BMI during this critical period of development. Indeed, few studies have taken a developmental perspective in order to understand how and when obesity develops in early childhood. By measuring BMI at multiple time points, we will examine growth trajectories in early childhood. This will allow us to examine the effect of a prevention program on these varying trajectories (Agras, Hammer et al. 2004; Pryor, Tremblay et al. 2011). As Barker et al. demonstrated, it is the change in BMI over time in early childhood, rather than BMI at any one time point, that is linked with health consequences in adulthood (Barker, Osmond et al. 2005). Moreover, an earlier childhood adiposity rebound is associated with an increased risk of later obesity (Rolland-Cachera, Deheeger et al. 1984; Cole 2004). Because clinical literature about childhood obesity indicates that the shape of the BMI trajectory across ages three to eight is curvilinear, we will account for this in our analytic plan (Kuczmarski, Ogden et al. 2002; Cole 2004) (see below).

Primary Analysis

Statistical model and approach

For our primary analysis, which will be an intention-to-treat analysis, we will fit the following quadratic mixed model equation (some subscripts suppressed for readability):

$$BMI = \beta_0 C + \beta_1 I + \beta_2 (age\text{-}X) C + \beta_3 (age\text{-}X)^2 C + \beta_4 (age\text{-}X) I + \beta_5 (age\text{-}X)^2 I + \ldots + error\ terms$$

where:

1. "I" is an indicator for group and equals 1 for the intervention group and 0 for the control group; "C" is an indicator for group and equals 1 for the control group and 0 for the intervention group; there is no intercept in this model in the 'traditional sense' (see point two below);

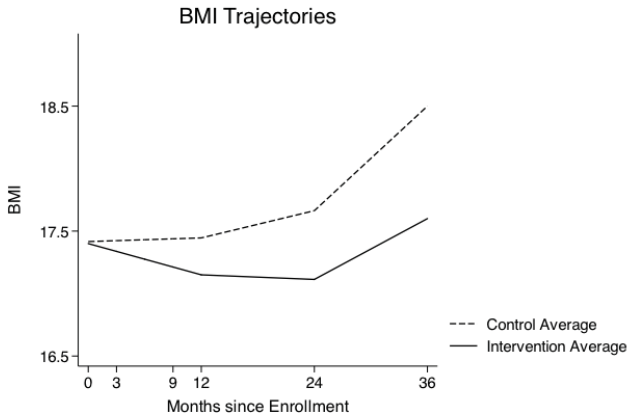
2. "X" is the value at which we center age; we plan to use age at enrollment as our centering term, which will make the indicator variables interpretable (β_0 as the mean BMI at enrollment for those in the control group and β_1 as the mean BMI at enrollment for the intervention group);
3. "..." stands for other predictors; at the present time, we believe that the predictors for the main model will be gender (coded, e.g., as 1 for female and 0 for male) and ethnicity (we expect there to be three ethnicity groups and thus two indicator variables for these); in addition, gender by age interaction terms will be included, since the literature indicates that trajectories may differ by gender;
4. For the primary analysis, "error terms" will include subject, subject X age, and the covariance between these random effects, using a heterogeneous variance structure for the fitted model (Roberts & Roberts, 2005). For the primary analysis, we will not include a random effect for subject X age^2, given that, with our proposed unstructured covariance matrix, the inclusion of this additional random effect would result in 13 random-effects components and may lead to convergence problems (see Rabe-Hesketh & Skrondal, 2012, page 348). We will examine the consequences of this choice via planned secondary analyses (see below, section 11.8)
5. A post-hoc test of whether will allow us to examine whether the quadratic terms differ between arms of the trial, thus answering our primary research question.

Interpretation of some terms: the indicator variable for trial arm, the linear term (age) for trial arm, and the quadratic term (age)^2 for trial arm jointly describe the trajectory (and starting point) for each group (intervention and control), and each can be interpreted as follows: the constant is the mean BMI at age on entry into the trial; the linear term indicates the rate of change at entry age; and the quadratic term indicates change in rate of growth (acceleration). In our specification, this model allows each child to have her/his own BMI intercept at baseline and own BMI trajectory. Accordingly, we do not include BMI at baseline as a predictor in our model. Additionally, we do not include a BMI by treatment interaction, because BMI is an outcome and treatment is a predictor. We plan to examine a baseline BMI by treatment interaction (as well as other interactions) in our secondary analysis (see below).

Our hypothesis is that β_5, the quadratic term for the intervention group, will be significantly different from β_3, the quadratic term for the control group, at the 0.05 level. We do not have a hypothesis about the linear terms. Note that we expect the sign of β_5 to be positive, and we expect the coefficient to be smaller than the coefficient for β_3.

A graphical view of the above description is provided below in Figure 11.1 (we have suppressed the lines for the individual age groups for readability); note that the actual model will produce smooth curves instead of the piece-wise linear curves shown in the graph.

Figure 11.1: Projected BMI trajectories over time



Assumptions with Justification

Assumptions Pertaining to Potential ICC among BMI Trajectories: We will have three waves of recruitment with 200 parent-child dyads/wave (100 dyads/arm). The control group will gather in unchanging groups in local libraries, where we expect little-to-no correlation even though children will stay in their original session for the entirety of the study. The intervention group utilizes a social network building component and will have pre-specified parent groups that will continue throughout the study. The intervention group will attend one of two community recreation centers (50 dyads/community recreation center/wave). Typically, we will divide these dyads evenly across three weekly sessions. The session is our subgroup (cluster) of interest. Each session will have approximately 17 families in it. If the size of the subgroup remains constant over time, the total number of subgroups we will have is 36, i.e., 600/(50/3).

It is also worth noting that we will further subdivide the 17 families of an intervention session into two smaller subgroups of 8-9 families. This division is done to facilitate our activities and encourage interaction among these smaller subgroups. It will also likely facilitate the development of social networks among these groups, which we hypothesize to be related to improved health outcomes for the treatment group over the course of our intervention. If we take this smaller subgroup as the unit for the intervention group, our total number of subgroups is 54, i.e., 18+36, or [300/(50/3)]+[300/(50/6)], where the first square bracket is the number of subgroups in the control group (where subgroups are not broken down into smaller subgroups), and the second square bracket is the number of subgroups in the intervention group.

The social networking aspect within the intervention group and the smaller group size lead us to predict a positive but small ICC that may be higher than what we expect to be a small ICC in the control group. Note, however, that session membership is well-defined for both the intervention arm and control arm, as participants will have minimal movement between sessions. This leads us to propose a heterogeneous variance structure for the primary analysis, allowing the ICC at the level of session to be estimated separately for the intervention and control arms.

Checking and Sensitivity Analyses: Once a model has been estimated, we will need to investigate its properties not only to ensure that any data idiosyncrasies do not impact the results but also to help ensure that the results are generalizable. The first issue is to check for systematic differences between the model and the data using graphs, such as comparisons of predicted and observed values of BMI, and other standard diagnostics (Snijders 2008). An extension of this idea is to simulate new sets of outcomes, based on our model, and use the simulated data as a reference test group by comparing this set to the observed result; in this case, we would look for situations in which the data appear different from what we would expect by using the model to predict the data (Gelman 2007).

A second issue is whether we have left out important features of the model, including, for example, (1) age at randomization, (2) measurement occasion, (3) study wave (by which we mean enrolled in first year, second year, or third year of the program), or (4) other demographic variables (e.g., SES, parent level of education) or substantive covariates (e.g., maternal depression). Some of these variables will be tested explicitly as moderators or mediators (see previous sections pertaining to moderators and mediators as well as sections 11.6 and 11.7 below). In addition, trajectories may vary by baseline BMI; this possibility will be checked by estimating a model with a baseline BMI by treatment group interaction. We will estimate additional models that include one or more of these additional features to check whether inclusion of any of these predictors is both statistically reasonable and affects our conclusions.

A third issue is whether age is correctly specified. With six data points, a limit exists as to what can reasonably be done. We suggest that the quadratic model should be checked in two ways: (1) substitute linear splines with a break between, for example, ages 4 and 5 (anticipated adiposity rebound timing); (2) substitute non-linear splines, in particular, restricted cubic splines with 4 knots chosen following Harrell's default positions (Harrell 2001).

A fourth issue relates to the potential correlation among the clusters/subgroups in our analysis: to what extent are these clusters correlated, what is the effect of that correlation on our results, and how accurately have we specified the clusters? Although we will not use the cluster-adjusted robust sandwich estimator in our primary analysis, we will, as a safeguard, fit a model that assumes a cluster structure within the data and compare the standard errors of this model to those from our primary model. If there are substantive changes in the standard errors, further work will be done to see which set of standard errors is more appropriate in our situation.

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

Estimated Attrition: Within each planned cohort of 200 dyads per three cohorts, six waves of data collection will occur, with shorter time intervals between the earlier waves and longer time intervals later. According to prior community-based studies, subject dropout decelerates over time, with the worst losses occurring early. We will make every effort to reduce attrition, with particular focus on the earlier waves of the study, to ensure that we retain at least 80% of our sample within each cohort, yielding a cohort size of at least 160 and a total sample size, at study end, of at least 480. This level of attrition would leave us sufficiently powered (.90) to be

able to detect a standardized effect size of .40 (a respectable and common effect size unique to the analytic method we are using--see sample size and power analysis section). An even larger sample size will increase the power to detect a meaningful difference, as explicated in the power analysis and sample size section below, and we will strive to ensure that the sample is as large as possible at each successive wave. In addition, it is important to note that our analysis is an intention-to-treat analysis. Accordingly, we will use all cases in our analyses, even those with as few as one wave of data, such that attrited cases will not truly be lost but instead retained in our analytic procedures.

Missing Data: Conceptually, we anticipate two types of missing data: (1) people who drop out after a measurement occasion and never return [i.e., lost to follow up]; and (2) people who miss one or more particular measurement occasions (e.g., occasion three) but are present for each of the others, at least one of which is later in time than the one (or more) that they missed.

With six repeated measurements, some participants inevitably will miss one or more occasions of outcome data collection. One advantage of the mixed models over older repeated measure ANOVA models is the use of all available data without dropping any subjects (Nich and Carroll 1997). We begin by assuming that the missing occasions meet MCAR or MAR assumptions (Little and Rubin 2002). If so, the results of the mixed model (e.g., the effect of time, group by time) are robust.

To guard against missingness biasing results, we will also conduct secondary analyses of missingness to see how realistic the assumption of MAR or MCAR may be. This check can be done in several ways. We will start with descriptive statistics comparing the characteristics of observations with and without missing values (e.g., gender, baseline BMI, age at enrollment, etc.). The first analysis will use standard multiple-imputation with 100 imputations (Little and Rubin 2002). Three possible directions, in addition to standard diagnostics (White, Royston et al. 2011) can be pursued when checking whether being missing is non-random (i.e., in checking the results of the multiple imputation):

1) The first method is our primary suggestion: we will impute the data using standard multiple imputation (MI) software but with constraints on the values that can be imputed. These constraints arise because our prime concern regarding non-random missingness is that either those who don't need the program (i.e., those who are lean) or those who perceive that they are not seeing an effect (i.e., who are, and remain, overweight) will miss occasions. For example, in one set of imputations we would constrain all imputed BMIs to be below, say, “a”; in a different set, we would constrain the imputed BMIs to be above, say, “b”; this type of constrained MI is discussed in An and Little(An, Little et al. 2010) and Jenkins, Burkhauser, Feng, and Larrimore(Jenkins, Burkhauser et al. 2011). One hundred imputations will be used for each such constrained MI. We will examine the BMI pattern of those who drop out and, if we see evidence of either "a" or "b", use the values we observe to set the constraints.
2) A second possible type of sensitivity analysis was originally suggested by Rubin (1987) and has been extended by Carpenter, Kenward, and White,(Carpenter, Kenward et al.

2007) who suggest weighting each imputed result (rather than Rubin's standard simple averaging of the results), where the weight depends on the assumed departure from the MAR assumption. Their technique relies on at least one strong assumption, but they provide a graphical diagnostic to help check this assumption.

3) If drop-outs (situation one above) are much more common than missing an occasion and then returning (situation two above), we will estimate a pattern-mixture model (Little 1993; Hedeker and Gibbons 1997). If missing one or more occasions and then returning is relatively common, however, we will not pursue this strategy.

Detectable Difference, Sample Size, and Power

Power and Sample Size Estimation: The power analysis was performed on our primary analysis (see below): a quadratic model of the BMI trajectories. For our sample size estimation, we used the OD (Spybrook 2011) software so that we would be consistent with our planned analysis. This software allowed us to examine two-group repeated-measures trials with quadratic change, the same model being used for the analysis.

This software uses a standardized effect size as defined in Raudenbush and Liu, namely, the group difference on the polynomial trend divided by the "population standard deviation of the polynomial trend of interest" (p. 391; the "population standard deviation" refers to the square root of the variance of the random effect) (Raudenbush and Xiao-Feng 2001). This specification, particularly the denominator, is quite different from cross-sectional standardized effect sizes such as Cohen's D, given that, with a polynomial model (here quadratic), the difference between groups depends on the point in time examined. In particular, given our hypothesis (see below), we expect that, after adiposity rebound is reached, the BMI of children in the intervention group will grow more slowly than that of children in the control group such that the differences between their mean BMIs will increase over time**.** Our expectation implies that we are interested in the significance of the quadratic term in the model, and expect that the difference between the control and treatment group quadratic effect will be significantly different from zero.

We note one difference between the OD program's assumptions and our study: the OD program assumes that the measurement occasions will be equally spaced over time, which is not the case in our study. As a result, specifications from the OD program may lead us to overestimate power and underestimate sample size. Power is high in the current study, as can be seen in the table below, thus we expect that these potential mis-estimations are not problematic.

To determine the power and effect size of the current study, we need estimates of the standardized effect size, which we obtained from a subset of our previous Salud Con La Familia study. We used only a subset of the Salud subjects because the inclusion criteria for that study (i.e., children at any level of baseline BMI) were broader than for the current study (i.e., children whose baseline BMI is between the 50th and 95th ([or 99th] percentile). For our estimations, then, we used only the Salud data for those from the 50th to the 95th percentile (and then again from the 50th to the 99th percentile [see below]). Other important differences exist between Salud and the current study, however, that limit our ability to estimate power and sample size based solely

on Salud: (1) the Salud subjects had only three measurement occasions which covered 15 months rather than six occasions over three years (the GROW trial) and (2) the Salud intervention was comparable only to the 12-week intensive phase proposed in the GROW study and did not include a maintenance or sustainability phase as proposed in the GROW trial. We expect that the increased number of sessions as well as the intensity of the intervention in the GROW trial will serve only to increase the power of the GROW study.

When using the OD software, the user can set various values, the most important of which is the standardized effect size discussed above. Other possible values to set include the duration of the study (here, three years), the number of measurement occasions (here six), and the variance of the residuals and the variance of the random effects. We found that even fairly sizable changes in value used for the residuals and the variance of the random effects had little effect on the projected sample size (e.g., holding other elements constant and changing the variance of the random effect of age-squared from the observed standard deviation of 2.8 [based on the Salud data] to the OD program's default of 1, only increased the sample size at a power of 0.8 by about 20 subjects). Using the program defaults for residuals and variance of the random effects was a conservative (i.e., produced larger estimates of sample size) approach compared to using the results based on Salud, thus we used these defaults in the table below. Changing the standardized effect size does have important consequences for the estimated sample size, however (see Table 9).

As previously stated, we used the Salud data to estimate our primary model (see below) for those within that study who were between the 50th and 95th BMI percentiles at baseline. The control group in the Salud data showed unexpected results with virtually no non-linearity (i.e., their BMI trajectories increased but in a linear fashion over a 15 month period), therefore we believe that the effect size from that model, which was quite large and based on different assumptions, is an overestimate of the effect that we will see in the GROW study. Instead we used the OD program default for the effect size of 0.4, a commonly used effect size in longitudinal studies and thus the OD program default, to estimate our required sample size. Accordingly, Table 9, below, indicates, for powers of 0.7, 0.8, and 0.9, the estimated sample size using the OD program for the default effect size (0.4) and for two additional effects sizes, a smaller and more conservative effect size (0.3) and a larger and more liberal effect size (0.5). As the table below indicates, we estimate that recruiting a sample size of at least 480 will leave us adequately powered to determine this middle/medium effect size of 0.4.

Table 9: Estimated required sample size for given standardized effect sizes

Power/Effect Size	Sample size for Standardized Effect size = 0.3	Sample size for Standardized Effect size = 0.4 *(OD program default)*	Sample size for Standardized Effect size = 0.5

70.00%	500	285	186
80.00%	640	360	232
90.00%	860	480	308

Because the results of our pilot study currently underway have led us to consider including children with higher baseline BMI in the GROW trial than we had originally planned, we also estimated our primary model on Salud participants who were between the 50th and 99th percentile of baseline BMI to determine the effects of including these children with a higher BMI. While, as expected, the variance increased when we moved to the model that added children between the 95th and 99th percentiles, the difference between groups (control and intervention) also increased such that the standardized effect size changed very little and, thus, there was virtually no effect on power (i.e., the desired sample size, under various conditions, never changed by more than two people). If, then, we decide to extend our criteria in the GROW trial to include children who are in the 95th to 99th percentile of BMI at baseline, our analyses will continue to be sufficiently powered.

Currently, the design for the GROW trial includes 600 children, and, though we would expect to be adequately powered at a smaller number of subjects, we plan to recruit 600 subjects to allow for potential attrition. We note, however, that if recruitment of that higher number of subjects becomes problematic (and we have observed in our current pilot study the difficulties inherent in recruitment for a similar prevention trial), we will stop subject recruitment at a smaller number of subjects, though ideally not less than 480 (see Table 9), such that we are adequately powered.

Analysis for Possible Effect Modifiers

The variables that are listed in the previous section as moderators (e.g., race/ethnicity, genetic risk score, etc.) will be entered appropriately into the analytic model as interaction terms in order to test the effect of the moderator on the outcome (child BMI trajectory). Relevant three-way interactions (e.g., child gender by age by group) will also be tested.

Analysis for Possible Effect Mediators

The variables that are listed in the previous section as mediators/covariates will be entered into the analytic model as time-varying covariates and their effects on the outcome will be assessed accordingly, controlling for all else in the model.

Secondary Hypotheses and Analysis

Secondary Analyses: We list below two sets of secondary analyses. The first is specific to our primary analysis (see Aim 1, Hypothesis 1); the second is specific to the secondary aims and related hypotheses (see Aims 2-6) and contained under section 11.9 (below).

Secondary Analyses in relation to the Primary Hypothesis and Analysis

1) Timing of adiposity rebound: We anticipate that we will be able to characterize and capture the timing of adiposity rebound for many of the children enrolled in the study. At time of enrollment, each child is at least three years of age and is less than six years of age (and we will know, including fractions, how old they are at enrollment by collecting their date of birth); measurement occasion six will occur at least three years after enrollment. Using these conditions, those who enroll on their third birthday will be at least six years old at measurement occasion six (and everyone else will be older); in this scenario it is reasonable to assume that most subjects who enroll at age three will have reached adiposity rebound by measurement occasion six, although we will miss some children who have earlier/later rebound timing. Also, virtually all children who enroll at age four should experience adiposity rebound during the study, but a few might be earlier than four or later than seven. Finally, the majority of those who enroll at age five should experience adiposity rebound during the study, but a minority will have rebounded prior to age five. Note that the mean age at adiposity rebound is a simple function of the coefficients from the main model: $-\beta_2/(2*\beta_3)$ will be the nadir for the control group (and a similar calculation captures the intervention group:

   $-\beta_4/(2*\beta_5)$).

2) The effect of parental change in BMI over the study period on child's growth trajectory: In this study, this effect will be modeled by including baseline BMI of the parent as a predictor, and also including other measures of parent BMI as time-varying covariates (i.e., the value of the covariate depends on the measurement occasion).

3) We will test the difference between mean BMI for both groups at the end of the trial (36 months) to determine whether they are significantly different from one another, thus adding additional information to our analyses.

4) We will test whether the trajectories of both normal and overweight children in the treatment group accelerate at a slower rate than those in the control group over time, such that those in the treatment group will be less likely to evidence trajectories of obesity compared to those in the control group. Each child will be categorized as having, or not having, an acceptable BMI trajectory. This binary variable will be the outcome variable for this secondary analysis. We will test this first, in an unadjusted analysis (a 2 by 2 table where one variable is the outcome variable and the other is group [control or treatment]), and then in an adjusted analysis using logistic regression. Predictors in the logistic regression will include demographics (e.g., gender) and various baseline variables, including the baseline BMI weight category (i.e., normal or overweight).

5) In a series of secondary analyses, we will examine the random-effects in more detail:

   1. Using our original fitted model, we will impose an independent covariance matrix (which assumes no correlation between random effects), reducing the resulting number of random effects from seven to five. The results of this change to the model will inform us about the next two steps (see below).

   2. We will add the two age-squared terms (for intervention and control) as random effects, continuing to use the independence structure, and bringing the number of random effects back to seven.

3. Keeping the two age-squared terms as random effects, we will return to an unstructured covariance matrix, bringing the number of random-effects to 13.
4. At each step in the above process, we will evaluate the results of continuing to add additional random effects terms, including noting model convergence problems. While we believe the model with 13 random effects will have reduced power and thus do not propose this model for our primary analysis, we believe that fitting this model in a secondary analysis, via the systematic steps outlined above, will allow us to examine the consequences of including a large number of random effects and determine the viability of this alternate model.
5. It is possible that in addition to different ICC's per condition, variability may occur across sessions within condition, such that a range of ICCs exists. If that range is determined to be sufficiently wide, we will consider adding cluster-adjusted standard errors for both the fixed and random-effects. Note that this type of standard error is a generalization of the traditional sandwich estimator; StataCorp has provided a FAQ on this generalization with citations: http://www.stata.com/support/faqs/stat/robust_ref.html.

Additional Analyses

Secondary Analyses in relation to the Secondary Aims and Hypotheses

In addition to the above analyses, we will conduct analyses necessary to support our secondary aims of the trial, as outlined below.

Aim 2: Compare the effect of the intervention in children who made significant changes in their dietary and/or physical activity behaviors to the effect in children who did not.
Hypothesis 2: Relative to children in the control condition, children participating in the treatment condition will:

2.1 Have lower sedentary activity levels (as measured by actigraphy data) after the intensive phase of the intervention (T2) and at study completion and/or

2.2 Have better adherence to age-specific USDA nutrition recommendations, (e.g., age-appropriate total calories increased, fruits and vegetables, decreased sugar sweetened beverages [measured via diet recall data]), after the intensive phase (T2) and at study completion.

Analysis:

(2.1) A multiple regression model in which child sedentary activity level is regressed on group, controlling for baseline sedentary activity level and including other relevant covariates (e.g., child gender), will be fit at T2 and at study completion.

(2.2) Each child will be categorized as evincing, or not evincing, adherence to age-specific USDA recommendations (as defined in the hypothesis). This binary variable will be the outcome variable for this secondary analysis. We will test this first in an unadjusted analysis (a 2 x 2 table in which one variable is the outcome variable and the other is group [treatment or control]), and

then in an adjusted logistic regression analysis predicting adherence category membership and including appropriate covariates (e.g., gender, baseline BMI) in addition to group.

Aim 3: Evaluate the effect of parents' physical activity levels and dietary behaviors on children's levels of the same.

Hypothesis 3: Parents who have significantly lower sedentary activity levels (compared to baseline) after treatment or who have better adherence to USDA nutrition recommendations (age-appropriate total calories increased fruits and vegetables, decreased sugar sweetened beverages [measured via diet recall data]) will be more likely than parents who have higher sedentary activity levels or who do not adhere to USDA nutrition recommendations to have children who will show

3.1: Decreased sedentary activity levels post-treatment and

3.2: Better adherence to USDA nutrition recommendations (as measured in 2.2, above).

Analysis:

Two binary predictors will be created denoting whether parents have significantly lower sedentary activity compared to baseline (yes/no) and whether they have appropriate versus inappropriate dietary adherence (yes/no). These dichotomous variables will be entered into models as follows:

(3.1) A multiple regression model will be fit at T2 and at study completion in which child's sedentary activity level is regressed on group, controlling for baseline child sedentary level, and including the parent dichotomous variables, and two two-way interactions between the parent variables and group (treatment or control) (and including other relevant covariates [e.g., gender]).

(3.2) A logistic regression model will be fit at T2 and at study completion in which the binary child adherence variable (see hypothesis 2.2) is regressed on group and including the parent dichotomous variables and two two-way interactions between the parent variables and group (treatment or control)

(and including other relevant covariates [e.g., gender]).

Aim 4: Explore the potential for developing new social networks and their effect on child nutrition and physical activity.

Hypothesis 4: Parents in the treatment group will develop new social networks and the strength of those social networks will be positively associated with reduced sedentary activity levels and improved dietary behaviors (measured as indicated above) among both parents and children.

Analysis:

A social network analysis will be conducted to determine the strength and cohesion of parents' reported networks. The effect of these networks on parental and child sedentary activity levels and dietary behavior will be estimated. Social network analysis will be conducted using the

software packages UCINET and In-Flow. UCINET will be used for entering and analyzing network data and, along with In-flow, for generating network measures and graphical displays. This data set will thus contain both network and attribute variables at the individual level of analysis. Applying standard statistical techniques (e.g., regression, logistic regression, etc.) these independent variables will be modeled with selected dependent variables. The analysis will examine the change in these social networks over time and their impact on the main outcomes of interest including: growth trajectories (children's BMI); body composition (child and adult), parenting practices (child feeding); physical activity (child and adult), and total energy intake. The social network hypothesis suggests that members of a given network group will share health behavior characteristics more than members of other groups.

Aim 5: Evaluate the moderating relationship between genetic risk factors and child BMI trajectories over the course of the study.

Hypothesis 5: Higher levels of child genetic susceptibility to obesity (i.e., a higher genetic risk score (Kathiresan, Voight et al. 2009)) will be significantly associated with heavier-for-age BMI at baseline, and this susceptibility will moderate children's growth in BMI over time.

Analysis:

"Heavier-for-age-BMI at baseline", the outcome, will be regressed on genetic risk score and the interaction between risk score and time, controlling for other covariates as deemed important (e.g., child gender, etc.).

Aim 6: Assess the degree to which implementation of the GROW program encourages additional lifestyle programming for preschool children and their parents in the Metro Community Centers.

Hypothesis 6: The two Metro Community centers participating in the GROW trial will implement a higher number of activity or nutrition programs for families (as defined by the centers) with young children at the end of the study compared to the number they implemented at baseline, and they will also implement a higher number after the study compared to the number implemented by non-participating Metro Community Centers.

Analysis:

A simple count of the number of activity and nutrition programs will be taken at baseline within both Community Centers (i.e., East and Coleman) and then again at the end of the study to determine whether the number at study end within each center exceeds that at baseline. Similarly, counts will be taken of these types of programs at non-participating Metro Community Centers at baseline and study end and these numbers will be compared to counts at both East and Coleman to determine if both participating centers have higher numbers than the non-participating centers at baseline and at study end.

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Revised Protocol

Specific Aims

This research includes one primary and five secondary specific aims:

Primary Aims:

1. **Aim 1:** Evaluate the efficacy of a multi-level intervention, addressing nutrition and physical activity, at public community recreation centers with high-risk parent- preschool child (ages 3-5) dyads to promote pediatric obesity prevention.
   1.1. **Hypothesis 1:** The BMI trajectories of children in the treatment group will accelerate at a slower rate than those in the control group over time.

Secondary Aims:

2. **Aim 2:** Compare the effect of the intervention in children who made significant changes in their dietary and/or physical activity behaviors to the effect in children who did not.
   2.1. **Hypothesis 2:** Relative to children in the control condition, children participating in the treatment condition will:
      2.1.1. Have lower sedentary activity levels (as measured by actigraphy data) after the intensive phase of the intervention (T2) and at study completion and
      2.1.2. Have better adherence to age-specific USDA nutrition recommendations, (e.g., age-appropriate total calories increased fruits and vegetables, decreased sugar sweetened beverages [measured via diet recall data]), after the intensive phase (T2) and at study completion.

3. **Aim 3:** Evaluate the effect of parents' physical activity levels and dietary behaviors on children's levels of the same.
   3.1. **Hypothesis 3:** Parents who have significantly lower sedentary activity levels (compared to baseline) after treatment and who have better adherence to USDA nutrition recommendations (age-appropriate total calories increased fruits and vegetables, decreased sugar sweetened beverages [measured via diet recall data]) will be more likely than parents who have higher sedentary activity levels and who do not adhere to USDA nutrition recommendations to have children who will show
      3.1.1. Decreased sedentary activity levels post-treatment and
      3.1.2. Better adherence to USDA nutrition recommendations

4. **Aim 4:** Explore the potential for developing new social networks and their effect on child nutrition and physical activity.
   4.1. **Hypothesis 4:** Parents in the treatment group will develop new social networks and the strength of those social networks will be positively associated with reduced sedentary activity levels and improved dietary behaviors (measured as indicated above) among both parents and children.

5. **Aim 5:** Evaluate the moderating relationship between genetic risk factors and child BMI trajectories over the course of the study.
   5.1. **Hypothesis 5:** Higher levels of child genetic susceptibility to obesity (i.e., a higher genetic risk score)9 will be significantly associated with heavier-for-age BMI at baseline, and this susceptibility will moderate children's growth in BMI over time.

6. **Aim 6:** Assess the degree to which implementation of the GROW program encourages additional lifestyle programming for preschool children and their parents in the Metro Community Centers.
   6.1. **Hypothesis 6:** The two Metro Community centers participating in the GROW trial will implement a higher number of activity and or nutrition programs for families (as defined by the centers) with young children at the end of the study compared to the number they implemented at baseline, and they will also implement a higher number after the study compared to non-participating Metro Community Centers.

7. **Aim 7:** Determine if obesity-related behaviors (physical activity, willingness to actively manage one's own health, weight loss) can spread through new social relationships (ACTIVATE).
   7.1. **Hypothesis 7:** After controlling for homophily (the tendency of individuals to be associated with similar others), and other confounding network effects, adults' changes in physical activity (as measured by accelerometry, activation as measured by the PAM, and weight loss as measured by BMI) will be associated with similar changes among other adults in their social networks.

8. **Aim 8:** For women who become pregnant during the GROW trial, to compare the trajectory of maternal gestational weight gain (GWG) in women exposed to the GROW intervention to women in the control condition (GROW Baby).
   8.1. **Hypothesis 8:** More women in the intervention will have a GWG trajectory that is consistent with IOM guidelines for appropriate GWG based on pre-pregnancy BMI.

9. **Aim 9:** To compare infant growth trajectories from birth through 6 months of life in infants of women exposed to the GROW intervention with infants of women in the control condition (GROW Baby).
   9.1. **Hypothesis 9:** Fewer infants of women in the intervention will have rapid weight gain in the first 6 months of life compared to infants of women in the control condition.

Background

Early childhood is a critical time for obesity prevention.

Changes in physical activity and diet, among many other factors, have contributed to epidemic levels of childhood obesity in the U.S.[1-5] Obesity rates have tripled among children and adolescents over the past thirty years[6,7], with Latino and African-American populations at disproportionately higher risk.[3,7,8] At the current rates of childhood obesity, 30 to 40% of today's children may eventually develop type 2 diabetes and reduce their life expectancy.[9] Nader et al demonstrated that children who were ever overweight during the preschool period were five times as likely to be overweight adolescents.[10] And the chances of overweight increases as the child ages. In that same study, 80% of school-age children who were ever overweight during this period went on to become overweight adolescents. The significance of mounting risk for sustained overweight and its consequences cannot be overstated. In the Harvard Growth Study, overweight adolescents as adults had a two-fold increase in all-cause mortality and an

increased morbidity due to cardiovascular disease.[11] It is not merely overweight/obesity in childhood that poses the risk for later increased mortality and morbidity as an adult, **the slope of early weight gain is a potent predictor**.[12,13] For example, Leunisson et al showed that rapid weight gain without concomitant growth in height during the first three months of infancy is linked with reduced insulin sensitivity in early adulthood. **Furthermore, Barker et al demonstrated that the risk of adult coronary events was more strongly related to the rapid childhood gain in BMI than to BMI attained at any particular age.[12] Consequently, this proposal will address prevention of rapid BMI gain during early childhood, fostering normal growth for those children who have a normal BMI (>50% and <85%) and improving BMI trajectories for those children who already have a BMI ≥ 85% <95% at ages 3-5 years.** There is little evidence documenting successful behavioral interventions to *prevent* early childhood obesity[14-16] and even less evidence concerning which factors may be crucial to success. Consequently, the Institute of Medicine (IOM)[17,18] and the *Strategic Plan for NIH Obesity Research*[19,20] call for a community-engaged, culturally-relevant, family-centered approach to obesity prevention that can be sustainable.

Family plays a crucial role in pediatric obesity prevention.

Family influences normative expectations of how and what to eat as well as how often to be physically active.[21,22] Moreover, families control the home environment that shapes children's early childhood choices, establishing behavioral habits.[23] For example, in the Viva La Familia study, random 24-hour dietary recalls of almost 1000 children showed that 67% of children's meals occurred at home and that most of these meals were high density, low nutrient foods, consistent with their parents' choices.[24] Parental involvement in programs to reduce overweight in children has been moderately successful, and is considered an important component of weight loss programs targeting children.[25,26] Many of these programs were focused on treatment, however, the same association appears to exist for prevention efforts as reported in a recent meta-analyses of randomized trials to prevent childhood obesity.[27] Parents' role appears to be as both models to their children and as active participants in creating a healthy environment that encourages healthy lifestyles. Children are nearly six times more likely to be physically active if their parents are physically active.[28]

One important component of parental involvement is the use of behavior change methods such as parent-child contracting to set clear goals for nutrition and activity and self-monitoring of caloric intake and activity.[26,29] Epstein's report of 10-year treatment outcomes for obese children indicates long-term success among families who used parent-child contracts to set clear goals.[26] In a 2006 position paper, the American Dietetic Association (ADA)[30,31] recommended that effective, developmentally appropriate pediatric obesity interventions include the following elements:

1) Parent training/modeling (involving behavioral counseling targeted at parents to improve their parenting skills);
2) Behavior modification training (involving goal setting, modeling, and self-monitoring);
3) Promotion of physical activity (including the reduction of sedentary behaviors); and
4) Nutrition counseling/education (including the provision of more general information on foods, shopping, and nutrition to promote healthful eating).

Obesity is impacted by both the physical and social environment.

It is not only the family that exerts influence over preschooler nutrition and physical activity habits, but both the physical and social environment.

Physical Environment: A developing area of research examines the impact of access to physical activity on increased activity levels. In a study by Wilson et al, access to physical activity such as neighborhood trails was associated with increased physical activity in low SES groups.[32] These same groups tend to have a higher likelihood of obesity.[33] Likewise, Sallis et al discovered that proximity of exercise facilities to one's home was associated with increased amounts of exercise.[34] Unfortunately, more physical activity barriers exist for residents living in poorer communities. For example, Estabrooks found that fewer free physical activity resources, such as parks and playground exist, in poorer communities.[35] Lack of affordable, safe, and accessible recreation facilities and programs have been cited as contributing to children's watching more TV at home, which in turn is associated with increased rates of obesity.[4,36] Creating links to free, accessible recreation would be especially important in areas where low SES populations live. **Public community centers provide access to physical activity for those populations at highest risk for obesity. Through our existing partnership between the Department of Pediatrics at Vanderbilt University Medical Center (VUMC) and Metro Parks and Recreation, we have the opportunity to conduct and test a community center based intervention that can reach this high risk population.**

Social Environment: Research now suggests that we have underestimated the influence of the social environment on shaping obesity-related behaviors. Social networks have been linked to obesity in adults and adolescents.[37-40] From a recently completed afterschool intervention (Gesell PI), we have initial support for our approach to spread physical activity through a newly developed network. Results indicated that children's existing friendships heavily influenced their routine level of physical activity. The strongest influence on the amount of time children spent in moderate-to-vigorous activity in the afterschool hours was the activity level of their immediate friends. Children consistently made adjustments to activity levels of 10% or more in order to emulate the activity levels of their peers (OR=6.89, p<.01). The child's own age (OR=.92, p<.10) and obesity status (OR=.66, p<.10) had statistically significant but relatively small direct effects on the individual's activity level. Gender had no direct effect on activity.[41] In another recently published study, we found that a new social network evolved among parents enrolled in a community-based obesity prevention RCT: Parents selectively formed friendship ties based on child BMI z-score, (t=2.08, p<.05), thus revealing the tendency for mothers to form new friendships with mothers whose children have similar body types.[42] Together, this work supports our proposition of utilizing the social influences of social networks that form during our intervention to amplify obesity-preventing behavior change. In the GROW intervention we will build new social networks through: frequent contact and facilitated interaction in structured small group activities.

Although the terms are often used interchangeably, social networks differ from social support. Social networks, the complex webs of social relationships and social interactions that connect individuals, have been shown to be strong influences on behaviors. Social support, however, is generally thought not to influence behavior, but rather be a mechanism to cope with challenges and facilitate recovery from illness, injury or disease.[43] Methodologically, social support is measured from the respondent's perspective to assess the support (e.g., emotional, cognitive, tangible support) an individual perceives to have, whereas social networks typically measure the

presence or absence of friendships and task- or work-oriented relationships (which may or may not provide support) and treats the ties themselves as objects of study.[44] Social network analysis allows us to see the whole group of individuals and their interconnectedness, and is in that sense broader than analysis of social support. Due to a dearth of data and to methodological challenges, there are fewer studies of how social networks affect health.

Genetic factors play a role in the development of obesity.

New research demonstrates a genetic risk score (GRS) is a potent predictor of BMI. Family studies have demonstrated that genetic factors account for anywhere between 40% and 70% of the population variance in BMI for individuals with severe obesity.[45,46] Until recently, specific genes contributing to BMI in the general population had not been identified. It is now clear, however, that certain gene variants exert a substantial, clinically important effect on BMI in humans.[47] The GIANT Consortium recently reported the results from large scale studies to identify genetic variants contributing to the risk of obesity in both children and adults. In January 2009, this consortium reported a meta- analysis involving over 100,000 patients, in which 8 obesity-related risk alleles were conclusively validated far in excess of the standard (5 x 10-7) for genome-wide statistical significance.[47] Moreover, whereas each particular obesity susceptibility variant confers only a modest effect on BMI, a genetic risk score summing each individual's number of susceptibility variants across all 8 genes is a more potent predictor of obesity.[47] All of the genes are on different chromosomes (unlinked), and therefore, were treated as an independent variable. Given that humans have two copies of every autosomal gene, each person has 0, 1, or 2 risk alleles at each locus, with a genetic risk score (GRS) ranging from 0-16 (for 8 genes, given 2 alleles per locus, maximum score is 16). Even in the general population, at the extremes of GRS, BMI ranges from 25- 27 are clearly associated with clinical obesity. A novel aspect of the present proposal is that it incorporates genetic data in relation to an interventional study to prevent early childhood overweight/obesity. It has now been conclusively demonstrated that specific genes predispose to obesity, yet their impact on early obesity prevention has not been studied. This critical question must be answered in order to translate the findings of genetic studies effectively into clinical practice.

Prevention must occur in preschool given that 60% of overweight preschoolers will go on to become overweight adolescents.[10] By conducting and testing trials in public community centers, exportable interventions could result allowing for a macro-level system change to address this expanding public health crisis. **Building on the success of an existing partnership between Vanderbilt Pediatrics and Metro Parks and Recreation in Nashville, TN, the team in this proposal will conduct and evaluate an intervention intended to prevent obesity in preschoolers in an approach that affects multiple levels of risk and is both family-based and community-centered. This research includes the following innovations:**

1. Evaluates the trajectory of early BMI gain, as directed by recent scientific discoveries.[12,13,48]
2. Conducts a pediatric obesity prevention trial based in public community centers that are routinely available to the populations at highest risk.
3. Addresses obesity in the understudied period of early childhood – when there may be an optimal opportunity to instill long term healthy lifestyles and BMI trajectories.
4. Assesses the macro-system level components of community centers and social networks and the micro-system level components of parent-child genetics on pediatric obesity prevention

5. Is an easily exportable intervention, and we are actively exploring the opportunity to do so with the National Association of Counties and the National Recreation and Parks Association.

Recruitment

We will recruit 600 adult parents-preschool child dyads (p/c dyads) to participate in this study for 3-years in duration ***(see appendix B for recruitment script)***. We will conduct a rolling recruitment and enrollment strategy for 18-months until a total of 600 parent-child dyads are enrolled. In order to preserve internal and external validity of the study, the success of any behavioral intervention is contingent on the researcher's ability to recruit and retain study participants. Successful retention of this longitudinal study begins at recruitment.

Recruitment efforts consist of a multi-pronged strategy including: site- specific recruitment at community pediatric clinics, WIC offices, Family Resource Centers and Read to Succeed/preschool sites, and Coordinated school health sites; study announcements on English and Spanish radio programs ***(see appendix D for invitation letter, language and scripts will be based from this letter)***; and bilingual study recruitment flyers ***(see appendix C for recruitment flyers)*** located at neighborhood organizational centers, Walmart, and other community agencies where families with young children gather (e.g., daycares, pre-K programs, churches). Due to a highly restrictive eligibility criteria of having a child's BMI needing to be in a certain range, we will conduct preliminary screens at a location convenient for the family that could include other community sites (approved by the IRB as a non-research performance site) or participants' homes, only if requested. In addition to these various approaches, we will also actively recruit in these other community agencies where families with young children gather. In addition, we will identify "community liaisons", well-respected persons considered deeply integrated in the community who have knowledge and relationships to easily reach and effectively communicate with our target population. Specifically, we will employ 3-6 community liaisons from each of the two communities (Northeast and South Nashville) to aid in recruitment and retention activities.

In order to assist in recruiting our hard-to-reach target population, we will also use Facebook as a viable tool for recruitment. Specifically, we will create a study-specific GROW Facebook page open to the general public that will serve as an online advertisement. All wording and language used for this Facebook page will be similar to our hardcopy flyers that will be disseminated in the community ***(see appendix C for recruitment flyers)***. This page will give interested participants the opportunity to message research staff who can then schedule a follow-up phone call or meeting. Research staff will also have an opportunity to post status updates on upcoming recruitment efforts, for example radio announcements or upcoming community-based events related to the GROW study. Facebook features such as the "like" feature will be enabled whereby individuals that choose to "like" the GROW study page will be updated via their newsfeed (the center column of an individual's homepage – a constantly updating list of stories from people and pages that they follow on Facebook) whenever our Facebook page updates our status. When individuals "like" this page, it also appears in their respective network's newsfeeds, thereby potentially exposing the GROW page to other prospective participants.

Participants in the GROW study will also be invited to aid recruitment efforts by voluntarily filling out the attached referral form at intervention or control sessions with the names, relationship and contact information of other families they may know with a child age 3 to 5. These referred

families would be contacted and invited to participate in the study by research staff either by phone or in person. For every family referred who participates in a screening conversation, the participant would receive a small token gift of appreciation valued at $5 (e.g., cooking utensils, key chain, Band-Aid holder, etc.). For every family referred that has met eligibility and are successfully enrolled in the study, the referring participant would receive a $10 gift card as a small token of our appreciation. Word-of-mouth recruitment has been an effective recruitment strategy in our formative phase work. Including small incentives for participants that successfully enroll other interested and eligible families, would serve as an additional strategy to assist recruitment efforts with our hard-to-reach target populations. The maximum number of gift cards participants will receive for this would not exceed $100 over the course of the 3-year trial.

From our GROW formative research pilot (IRB No. 100591), out of 439 parent/child dyads assessed for eligibility, only 50 parent/child dyads were eligible and participated at baseline; a 10% return on investment. Due to the challenge of enrolling in a large, longitudinal, community-based, prevention trial, another strategy of recruitment will include outreach to patient families seen by either the Vanderbilt Pediatric Primary Care Clinic or surrounding community practices. To improve efficiency in light of our restrictive eligibility criteria, we will use Vanderbilt's StarPanel, a computerized electronic medical record database and Vanderbilt's Whiteboard, a scheduling database, to generate lists with scheduled clinic dates of potential participants that meet BMI, age and zip code eligibility criteria.[94] Specifically, clinic staff will provide a list of participants to research staff that meet eligibility criteria which serves as a pre-screen to identify targeted, potentially eligible, participants and invite them into the trial. With these lists, we will also send out an invitation letter to prospective participants that includes an opportunity to opt-out recruitment efforts whereby these families that do not wish to be called or approached in clinic's waiting room, may contact research staff to opt out of receiving any recruitment phone calls or being approached on-site at clinic ***(see appendix D for the invitation letter and D1 for invitation letter in Spanish)***.

The Monroe Carell Jr. Children's Hospital at Vanderbilt Division of General Pediatrics serves families from Davidson County, caring for a panel of 15,000 patients, many of whom reside in the zip codes of interest (refer to letter of support). Ninety percent of patients qualify for Medicaid. Moreover, the Cumberland Pediatric Foundation, including more than 200 community pediatricians in middle Tennessee, will refer eligible parent-child dyads to the study (refer to letter of support). The majority of children served in these clinics are 5 years old and younger presenting for well-child examinations. Utilizing this multi-pronged, recruitment strategy, we plan to reach our required numbers of study participants.

In addition to the recruitment process, the prescreening process has been developed to assess major elements of eligibility criteria at all recruitment sites ***(see appendix E for prescreen survey (English version) and appendix F for prescreen survey (Spanish version)).*** Moreover, recruitment for a few additional sub-cohorts (i.e., ACTIVATE, or GROW Baby), will include leveraging existing GROW trial participants, whom are eligible and interested. These cohorts are all designed to minimize participant burden.

Informed Consent

For the GROW trial, informed consent will be obtained on the same day of baseline data collection. Prior to obtaining the informed consent, adult parents and their preschool-aged child will conduct a brief eligibility screening, specifically, re-measuring height and weight to confirm

the eligibility requirement of the child's BMI ***(see appendix G for script for consenting with children)***. If the child participant meets BMI eligibility criteria (≥ 50% and <95%) then the child will be escorted to an on-site child activity room, while the parent will be invited to initiate an informed consent process. In order to minimize participant burden and maximize accuracy, we may use the child's height and weight prescreening data. Consent for use of this prescreening data will be obtained by parent as part of the consent process *(see Consent Form).*

Families that do not meet the eligibility criteria will receive a small token of our appreciation of their time and would not be eligible to participate for the specific cohort recruitment period; however if they become eligible for future cohort recruitment periods, they could be reassessed. Participants that do not meet eligibility criteria, data will be destroyed. During prescreen and prior to baseline data collection, participants have the option to receive information via a variety of mediums: phone, text or email. Text messages will be implemented by research staff following phone call contact to remind and confirm upcoming scheduled appointments with our hard-to-reach target participants, if they so choose.

Informed consent will be obtained in a private space within a public meeting place of the community center before the initial baseline measurements. While both parents and all in the family are invited to attend sessions, only one adult (either mother or father) will be present for the consenting process and enrolled in the program, since the parent or legal guardian must be willing to commit to the 3-year study (see 11E below for eligibility criteria). During the consenting process, the child will be escorted to the childcare room located in another room at the community center.

For all consent forms, we will ask participating adults if they would prefer to use English or Spanish to understand their role in the research study. With their language of preference, informed consent forms will be handed to participating adults and then read and reviewed in the language of preference. We model our current informed consent on our recently completed study (IRB No. 100591). We include some critical questions to ask parents to ensure they understand the consent form before signing it. If the participant gives consent, they will sign and date one copy of the form and keep another for their reference; both forms are also signed and dated by the study team member obtaining the informed consent.

Inclusion Criteria:

Eligibility inclusion criteria for participation in this study are as follows:

- Three-to-five year old children
- English- or Spanish-speaking
- Child's BMI ≥ 50% and <95%
- Parental commitment to participate in a three year study
- Consistent phone access
- Parent age ≥ 18 years
- Parents and children must be healthy (parents with controlled medical conditions will also be eligible)as evaluated by a pre-screen ***(see appendices E & F)***
- Child completion of baseline data collection on height and weight, two diet recall sessions, and at least 4 days of accelerometry and all willing survey items completed by the parent
- Racial and ethnic minority populations disproportionately at-risk for developing obesity

- Dyad must be considered underserved which will be indicated by the parents self-reporting if they or someone in their household participate in one of these programs or services: TennCare, CoverKids, WIC, Food Stamps (SNAP), Free and Reduced Price School Lunch and Breakfast, Families First (TANF), and/or subsidized housing.
- Residence in or recruitment from one of two Nashville regions: **East Nashville/Region 1 (37206, 37207, 37208, 37213, 37216, 37228, 37189, 37115)**: surrounding the East Community Center and **South Nashville/Region 2 (37013, 37204, 37210, 37211, 37217, 37220)**: surrounding the Coleman Recreation Center

For the purposes of this study we define the participating index "parent" as the legal guardian of the child who identifies that they spend the majority of time with that child at home. Other family members (e.g., grandmother, uncle/aunt, etc) may be recruited and enrolled in the program only if they have been granted legal guardianship via court order. During the consent process, legal documentation will be requested and stored for documentation purposes.

Per COPTR requirement, certain baseline data collection measures must be successfully completed prior to randomization. Once height and weight, at least two diet recall sessions, and at least four valid days of accelerometry from the child are completed, and all survey items families are willing to complete have been collected, parent-child dyads will be grouped into strata according to parent dominant language preference (English versus Spanish). After these requirements have been successfully completed, dyads within the strata will then be randomized to the intervention and control treatment groups.

For the sub-cohort studies, informed consent will be provided at pre-existing data collection time-points.

For the GROW Baby Sub-Cohort, eligibility criteria are as follows:

- Mothers must be enrolled in the GROW Trial, thus meetings its inclusion criteria
- Women must report a pregnancy and have a minimum exposure of six hours to the behavioral intervention or enrolled in the control condition for at least 6 weeks

For the ACTIVATE Sub-Cohort, eligibility criteria are as follows:

- Any GROW parent participant that attend a T5 or T6 data collection time-point.

Exclusion Criteria
For the GROW trial:

- Children who are <50% BMI or ≥ 95%
- Children outside the specified age range
- Families who do not speak English or Spanish
- Lack telephone contact
- Lack parental commitment to participate consistently for a three-year period
- Parents and/or children who are diagnosed with medical illnesses where regular exercise might be contraindicated and are not controlled
- Children who display dissenting behaviors during baseline data collection
- Parents/children who do not otherwise meet the eligibility criteria listed in section above as determined by pre-screen

For the GROW Baby Sub-Cohort, exclusion criteria are as follows

- Mothers are pregnant with multiples (i.e., twins, triplets)
- Mothers suffer a spontaneous abortion or fetal loss
- Mothers are diagnosed as having a high risk pregnancy that cannot be managed conservatively
- Infants will be excluded if their estimated gestational age is <36 weeks
- Infants have a genetic or medical condition that would significantly alter infant growth (e.g., Trisomy 18)

Inclusion Statement: **The GROW study operationally defines participants using the following inclusion criteria:**

GROW Child: Developmentally normal three-to-five year old children with a BMI ≥ 50% and <95%.

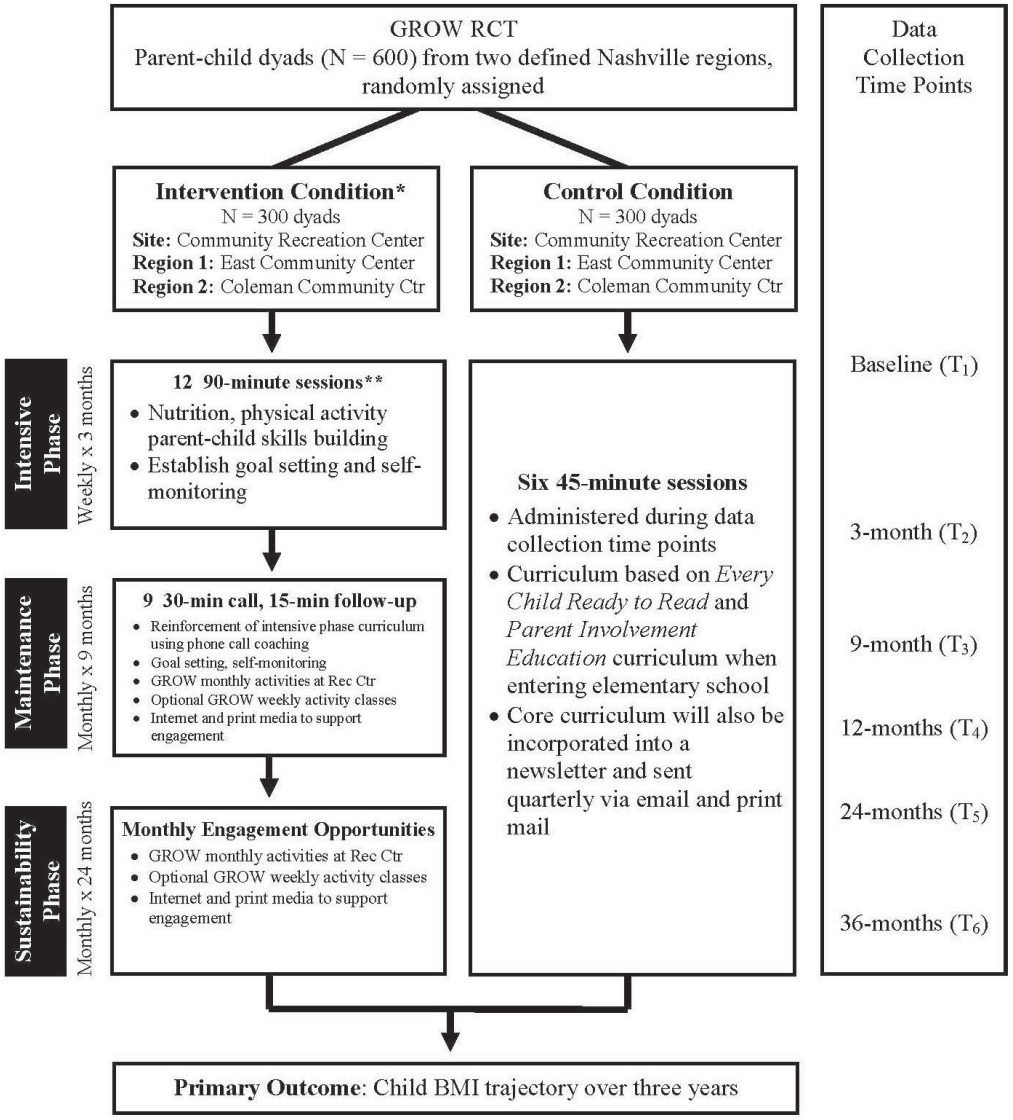
Adult: Healthy adults age 18 or older and designated as the child's parent or legal guardian. We will also include adults that have *controlled* medical conditions given that mild-to-moderate physical activity leads to overall well-being. The informed consent includes information on potential risks of mild to moderate activity including a statement that encourages participants to consult their healthcare provider if they are unsure of the safety of engaging in mild-to-moderate physical activity. All suggested exercises will be mild and are unlikely to cause injury.

Family: Speaks English or Spanish, resides in the defined vicinity of the intervention community center or control library, has a commitment to the 3-year study, has phone access, and resides in a household that participates in an assistance program for the underserved (e.g. TennCare, WIC, SNAP, free/reduced price school lunch).

Study Procedural Overview

Figure 1: GROW Trial RCT Study Phase

GROW RCT Design



*The intervention group will also receive control content
**All intervention sessions will include a tested curriculum with groups of up to 17 dyads and will promote social network development

We will conduct a rolling recruitment and enrollment for 18-months until a total of 600 parent child dyads are enrolled.

Study Treatment Groups

The intervention group will have three phases: 1) an intensive phase (weekly for 3 months) on nutritional, physical activity and parenting skills-building via 90-min in-person sessions that promote new social networks (see appendix O for GROW Curriculum and refer to modules attached). One example of a module would be setting family goals around nutrition and physical activity. We provide encouragement to utilize the built-environment for routine family physical activity and access to healthy foods using internet/mail media, email and mail media; 2) a

maintenance phase (monthly for 9 months) via 30-min phone coaching calls to reinforce concepts from phase one (see appendix I) and a brief 15-min follow-up call one week later (see appendix J), continued encouragement through internet and mail media, the availability of weekly activity programming for parent-preschool child dyads through the recreation centers, and monthly 60-minute GROW events for families to reinforce key messages; and 3) a sustainability phase (monthly for 24 months), where there is a discontinuation of phone call coaching and continuation of the other elements from phase two. In addition, for the intensive phase only, families can select receiving their information via a face-to-face or coaching phone call sessions (see intervention modules for content and scripts). These phone call sessions will be 20 minutes in length due to the exclusion of the small group discussion, hands-on activity with GROW child, and cooking activity, generally included in the face-to-face, in-person sessions.

The three main pillars of behavior change will be applied at each face-to-face and phone coaching session: 1) goal setting; 2) self-monitoring to achieve those goals; and 3) problem-solving. Additionally, after each measurement point in the intervention group, both the parent and child participants will receive a feedback report on growth in the form of an age and gender-appropriate BMI curve with an explanation of how their child is growing as well as their own BMI information with an explanation.

Intervention and control participants will receive a 45-minutes school readiness/school success program during each of the 7 data collection points. Both conditions will receive a quarterly school readiness/school success newsletter that will go out via email and snail mail over a period of 3-years. The core curriculum will be incorporated in the newsletters and will involve developing parental skills while also creating a practice-based learning environment for parent-child dyads around school success utilizing key elements of Every Child Ready to Read,95 a project of the Association for Library Service to Children and the Public Library Association (see appendix P for the Control Curriculum. As children age in the study and enter elementary school, the control parent-child dyad will receive a curriculum that integrates core elements from the Parent Involvement Education curriculum, tested and implemented by the Parent Institute for Quality Education (PIQE) to improve school success.96 During the beginning of the study, 1-2 field trips will be held to expose families to local public library facilities, encouraging their use of library resources, and introducing them to library staff. In addition to the quarterly newsletters, control family participants will be receive a calendar of monthly library events (via email and snail-mail) in order to continuously engage families to resources that integrate the core curriculum into their built-environment at the public libraries.

Similar to the prescreening process and for the convenience of our study participants, text messages will be implemented by research staff to remind them of upcoming sessions and provide them with information relevant to the study aims (i.e., promoting family-based healthy lifestyles and/or school readiness/school success). If participants would prefer not to be contacted via text (i.e., text message costs, unreliability, privacy concerns, etc), then we would refrain from doing so and identify other appropriate means to contact them based on their preference (i.e., phone calls, newsletters, face-to-face, etc). See Recruitment Eligibility Form for questions on best way to contact families.

Data collection sessions will be conducted for both treatment groups at 6-points in time (T1-T6): baseline, 3-months, 9-months, 12-months, 24-months, 36-months, and one at 48-months. Each of the six data collection points in this study will be conducted on-site at either community recreational center (i.e., Coleman and East Park) with Metro Parks staff and research staff. Metro Parks staff will not be "engaged" with research but will handle flow, childcare and check-

in with participants. This data collection process will involve adult-child dyads to proceed through a variety of stations to gather measurements and information for study analysis. In addition, make-up data collections sessions will be available for families in all data collection points. These will occur at a location convenient for the family that could include other community sites, approved by the IRB for recruitment, and/or participants' homes. Additional data collections collected yearly will be optional for existing participants (T7 & T8). Like before, we will obtain consent prior to collecting data at these additional data collection sessions. In addition, we will request permission to link child health data to school-related outcomes (i.e., attendance and test scores).

Social media use throughout the study for the Intervention Group

Since our targeted population are underserved families, such families have been well-known in the literature to be hard-to reach and hard-to-keep families, especially over a 3 year period of time. Because of this challenge, Facebook has been considered a viable tool to retain and reach families, in addition, serve as an interactive tool to continually maintain engagement for participants in the GROW study (see appendix H for Facebook messages). Thus, all study participants in the intervention groups will be invited to use a social media platform (grow-program.com). Specifically, participants will receive reminders to upcoming sessions/community events, polls to gauge satisfaction and curriculum understanding, posts that display recipes, pictures, and videos, and links to helpful web links for more information. In addition, participants will be able to post comments and pictures, and potentially strengthen their social network ties amongst themselves. Per Vanderbilt Social Media Policies, research staff will monitor content daily to ensure appropriate discourse and interaction that uphold the standards of Vanderbilt as an institution. For those families that do not have access to this tool, emails and/or regular mail will be sent out monthly. See attached for our re-engagement letters (in both English and Spanish) that will be sent to families that have been lost in the study. An additional letter (back-up) is sent out if there remains no response from these study participants.

The Adaptive Intervention Design

The research team plans to utilize an adaptive intervention approach97 for children who are not responding to the intervention based on their BMI trajectories. More simply, for the purposes of this adaptive intervention, a child will be considered a non-responder if her/his BMI weight categorization shifts negatively from T1 to T2 (i.e., if formerly normal weight child shifts to overweight or obese in this period of time; or if formerly overweight child shifts to obese, as defined by BMI). Child BMI change from T1 to T2 will be reported using an easily understandable and comprehensive growth feedback report and mailed to the parents after T2 measurements are collected. The adaptive intervention will occur at the first phone call coaching session of the maintenance phase. The coach will review the feedback report with the parent and solicit from the parent both the successes and barriers faced with incorporating GROW lessons into their everyday lives (responders will also receive feedback reports but will not receive a report explanation session discussed by a phone call coach). These adaptive intervention report feedback sessions will occur again after BMI categorization/non-responder status is reassessed at the T3, T4, and T5 data collection time points.

The Pregnancy Sub-Cohort (GROW Baby)

The research team will develop a prospective cohort of women who become pregnant during this ongoing GROW behavioral intervention, designed to prevent childhood obesity in minority and underserved families. During the trial, if any mother reports a pregnancy, we will invite them to participate in this new cohort. In order to determine how maternal prepregnancy BMI, maternal gestational weight gain, and early infant feeding practices interact to shape infant growth trajectory in the first six months of life, this research team will obtain 1) data on feeding

practices between 3-4 months of child's life via a phone call survey; and 2) data from chart reviews (OB records and pediatric records), using previously validated abstraction forms for both pregnancy characteristics and infant growth. The phone call survey has 24 items and will take approximately 10-15 minutes to complete. Medical records will be obtained from OB/GYN offices, pediatrician offices, and hospital delivery records. Mothers will sign a release of medical information for relevant charts, which will be facilitated through the Vanderbilt Clinical Trials Center. These data will be compared to other baseline demographics, maternal co-variates of interest and pre-pregnancy anthropometrics (see Pregnancy Cohort Data below for details on data sources). The development of this type of cohort will provide an opportunity to combine research-quality anthropometrics and co-variates, already being prospectively collected with additional patient-reported outcomes and anthropometric measurements, in a natural experiment to address important questions about pregnancy health and pediatric obesity prevention in the early stages of life.

The Social Network (ACTIVATE) Sub-Cohort

During T5 and T6 data collection, the GROW Trial has already been approved by Vanderbilt's IRB to administer the Social Network Survey (see appendix L) that will ask participants to name up to seven GROW study participants that they consider friends (friendship network). Since all participants will be asked the same questions, a mapping of the social network will emerge in the data. From these data we will also be able to weight ties according to strength of friendship or frequency of communication. Subsequently, in addition to the Social Network Survey, all families that attend T5 and T6 data collection will be invited to participate in an additional survey entitled the Patient Activation Measure (PAM), see measures section below for more details. The PAM survey, a previously validated measure,98 is deigned to elicit individual's knowledge, attitudes, skills and confidence in self-managing health. Higher PAM scores suggest that individuals are more likely to understand that their active involvement is critical to their health. Data from both surveys will help determine if obesity-related behaviors (i.e., physical activity, willingness to actively manage one's own health, weight loss) can spread through new social relationships. Prior to administering the PAM survey, informed consent will be obtained for all interested participants (see attached consent form lead by Dr. Sabina Gesell from Wake Forest). Families that agree to consent will then be enrolled in this ACTIVATE sub-cohort.

Outcome Measures & Procedures

In addition to BMI as the primary outcome variable, we have seven *a priori* secondary outcome variables, which were specified after the study began, but before the non-baseline data were unblinded by arm. Four are related to diet: average daily energy intake (kcal), percentage of energy intake from fat, carbohydrates, and protein. Two are related to physical activity: average daily time (minutes) spent in rest and sedentary behavior, and moderate and vigorous physical activity. The seventh variable is parent community center use with child (never versus at least once).

Process Measures

The GROW trial process measures will include: participation rates collected via attendance logs; data collection process collected via timed logs and identification of any issues that arise during the data collection procedures; retention barriers and facilitators via call logs conducted by the

study team; session fidelity checks to ensure consistency and accuracy of content administration; logs to assess use of recreation center and library outside of mandatory GROW-related sessions; Metro Parks and Recreation facility staff satisfaction surveys to assess barriers and facilitators of conducting the research program within their facility; library facility staff satisfaction surveys to assess barriers and facilitators of conducting the research program within their facility; and parent-child satisfaction with study participation. The GROW Trial will also administer a brief survey to intervention participants to identify participants' preferences on the types of programming delivered by community recreational centers to encourage and sustain use of their built environment for physical activity (See Appendix S for survey).

Collection of Moderators & Mediators

Conceptually, moderators identify on whom and under what circumstances the study treatment have different effects. In contrast, mediators identify why and how the treatment works or doesn't work. Below is a table including all moderators and mediators identified for this study, the measurement tool, a brief description, the intended respondent, method and time point of data collection. ***See Table 1: Collection of Moderators & Mediators below for details.***

Note: Computerized surveys are electronic surveys from the REDCap Database that will be administered and completed at the community center; no procedures will be conducted at Vanderbilt nor at home. Once entered and saved, the data will be housed on a Vanderbilt server. REDCap provides the ability to enter measurement data, including basic mathematic and logic checks for verifying valid data, as well as survey data. The research staff will utilize a combination of the wireless internet at the community center and mobile hotspots to provide internet access for all computers used.

Table 1: Collection of Moderators & Mediators

Domain	Measurement Tool	Description	Respondent [Parent (P) or Child (C)]	Method	Collection Time	Site-Specific?
Physical Activity	Accelerometer (GT3X+)	Sedentary activity (% sedentary mins/total wearing time)	P, C	Parent and child accelerometer wear (≥4 days, ≥6 hrs/day)	T_1, T_4, T_5, T_6	No
	GROW developed survey questions related to intervention messages	Self-reported physical activity habits	P	Computerized Survey (3Q)	T_1 , T_2, T_4, T_5, T_6	Yes

Nutrition	Diet Recall (child only) Survey Item GROW developed survey questions related to intervention messages	Total calories and macronutrient content (% fat, protein, carbohydrate) adherent to USDA recommendations Parent and child eating and feeding habits	P P	3-day child diet recall (parental report for child) Computerized Survey (9Q)	T_1, T_4, T_5, T_6 T_1 , T_2, T_4, T_5, T_6	Yes No Yes
Social Network	GROW developed Social Network Survey	Assessing social networking and its influence on behavior modification	P	Computerized Survey (11Q)	T_1 , T_2, T_4, T_6	Yes
	Bollen & Hoyle Perceived Cohesion Scale	Assessing group cohesion	P	Computerized Survey (6Q)	TWeek 3, Week 6, T_2	Yes
	GROW developed Advice Scale	Assessing information sharing	P	Computerized Survey (2Q)	TWeek 3, Week 6, T_2	Yes
Parenting Practices	Toddler Feeding Questionnaire (TFQ)	Parenting approaches to child feeding	P	Computerized Survey (34Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Eating Behaviors	HHHK - Eating Behaviors subscale	How often meals are eaten together	P	Computerized Survey (3Q)	T_1 , T_2, T_4, T_5, T_6	No
	GROW developed survey questions related to intervention messages	Where meals are eaten together	P	Computerized Survey (4Q)	T_1 , T_2, T_4, T_5, T_6	Yes
	Brief Motivational Interviewing (BMI)	Child and adult eating out	P	Computerized Survey (8Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Sleep	GROW developed survey questions related to intervention messages	Parent and child sleeping habits	P	Computerized Survey (6Q)*	T_1 , T_2, T_4, T_5, T_6	Yes

Media Use	Stanford (GEMS/ ECHALE) developed questions	Media available in household	P	Computerized Survey (3Q)	T_1 , T_2, T_4, T_5, T_6	No
	YRBS subscale	Child's media use	P	Computerized Survey (3Q)	T_1 , T_2, T_4, T_5, T_6	No
Use of Rec Center	GROW developed survey questions related to intervention messages	Parent and child knowledge and use of rec center outside of GROW activities	P	Computerized Survey (3Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Use of Library	GROW developed survey questions related to intervention messages	Parent and child knowledge and use of libraries outside of GROW activities	P	Computerized Survey (9Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Perception of the Built Environment	Participant Physical Activity and Neighborhood Supports Survey	Parent knowledge of the resources in the built environment	P	Computerized Survey (57Q)	T_1, T_4, T_5, T_6	Yes
Stress	Cohen's Perceived Stress Scale (PSS)	Assesses current levels of parental stress	P	Computerized Survey (10Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Depression	Center for Epidemiological Studies-Depression Scale (CES-D)	Assesses levels of parental depression	P	Computerized Survey (21Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Goal Setting and Monitoring	GROW developed survey questions related to intervention messages	Ability to set and track goals	P	Computerized Survey (6Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Executive Functioning	Stephanie Carlson's Executive Function Scale for Preschoolers	Comprehensive executive functioning measure	C***	Hands-on Tasks (about 10 mins)	T_1, T_5	Yes
Weight Perception	COPTR common survey questions	Current perception of parent's and child's weight	P	Computerized Survey (2Q)	T_1 , T_2, T_4, T_5, T_6	No
Self-Efficacy	Parenting Sense of Competence (PSOC) and Perceived Competence Scale (PSC)	Confidence around parenting decisions	P	Computerized Survey (13Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Readiness to Change	Brief Motivational	Assesses parent's	P	Computerized Survey (6Q)	T_1 , T_2, T_4, T_5, T_6	Yes

	Interviewing (BMI)	readiness to change around healthy eating and physical activity				
Child Asthma/ Allergies	GROW developed survey questions	Child asthma history and allergies	P	Computerized Survey (2Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Well-Being	SF-12	Adult general well-being	P	Computerized Survey (1Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Smoking	NHANES 2011-2012	Adult Smoking Practices	P	Computerized Survey (1Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Child Healthcare	GROW developed survey questions	Child health insurance and healthcare visits	P	Computerized Survey (4Q)	T_1 , T_2, T_4, T_5, T_6	Yes
Demographics	Demographic questions	Common and site-specific demographic questions	P	Computerized Survey (15Q Common; 6Q Site-specific)	T_1	No**
Genotype	Oragene kit (adult), baby brush (child)	Genetic risk score	P, C	Genotyping saliva	T_1, T_6	No
Family Health History	Brief Motivational Interviewing	Known family health problems	P	Computerized Survey (5Q)	T_1	Yes
Perinatal Health	Updated questions from KA Dept of Health WIC intake	Maternal gestational health, birth weight, and breastfeeding habits	P	Computerized Survey (7Q)	T_1	No**
Health Literacy	The Newest Vital Sign (NVS)	Understanding food label information	P	Computerized Survey (5Q)	T_1	Yes
Food Security	USDA 2008 subscale	Financial barriers affecting availability of food in the home	P	Computerized Survey (7Q)	T_1, T_5, T_6	No
Intelligence	Woodcock-Johnson III Tests of Cognitive Abilities – Brief Battery	Standard intelligence measurement	C***	Three 5-10 minute hands-on subtests	T_1	Yes

Q = Survey Questions
*** Some accelerometry data will be used to assess sleeping behaviors.**
****Some site-specific questions have been added in addition to the common questions in these areas.**
*****Executive functioning and intelligence will be administered to children who are 4 and 5 years old at baseline.**

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Description of Measures

Anthropometric Measurements

Body weight for each subject will be measured, after voiding and wearing light clothing, to the nearest 100 g on a calibrated digital scale. Body height without shoes will be measured to the nearest 0.1 cm with a stadiometer. BMI will be calculated (weight [kg]/height [m^2]), using the standard CDC calculator. Both height and weight measures will be collected twice. The mean of the two closest measures is used as a final measurement. Children will be wearing light clothes and without shoes. Height without shoes will be measured to the nearest 0.1 cm using our standard stadiometer (Perspective Enterprises, Portage, MI). Adult and child waist circumference will be measured with a fiberglass measuring tape on the skin, at the umbilicus, to the nearest 0.1 cm, according to the recommendations of the World Heart Federation.[99] Waist circumference will be collected two times, if the two measurements of waist differ by 1 cm or more, then the waist measurements are repeated a third time and data entered. The mean of the two closest measures is used as a final measurement. Measurements will be obtained by trained project staff and standardized according to accepted standards.[100-102]

Triceps Skinfolds

Triceps skinfold thickness is a measure of subcutaneous fat and is a component of equations used to predict body fat composition.[103] SFs have been used successfully in studies with adults and children,[104-106] including young children from 3 to 8 years of age.[107,108] Recent literature suggests that SFs are more accurate in estimating body composition compared to bioelectrical impedence (BIA) during the adiposity rebound, the normal pattern of growth that occurs in all children growing between 3 to 5 years of age.[107] SF is measured using a 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 project of the acromion process of the scapula (shoulder blade) and the inferior margin (bottom) of the olecranon process of the ulna (elbow). They are measured to the nearest 0.1 mm and collected two times. A third SF measurement is taken if either of the following occur: 1) If the two triceps values are less than 10mm but differ by 2 mm or more; or 2) If the skinfold is 10mm or larger, with a difference between the two measurements of greater than 10% (((maximum-minimum)/minimum)*100). In either case, the mean of the two closest measures is used as the final measurement. In order to accommodate participants that are morbidly obese participants then we will use the Harpenden calipers. Training, certification and quality control procedures for SFs are similar to those outlined above for waist circumference and other anthropometrics.

Accelerometers

Amount of physical activity will be assessed using the ActiGraph GT3M (Actigraph LLC, Ford Walton, FL) accelerometer. Accelerometry had been used successfully in studies with adults and children[109-113] with a reliability: r = 0.93 [114] . Both a parent and a child will be asked to wear the monitor for one week during waking and sleeping hours except when bathing, showering, or swimming. A simple 1-page manual (in Spanish and English) will be provided. The monitor will be attached to a belt secured at the waist. The monitors will be sent by mail in pre-addressed and pre-stamped boxes to the Energy Balance Laboratory at Vanderbilt. We have used this technique very successfully in similar studies with children and their families. The activity data will be downloaded to a computer and analyzed. Physical activity will be expressed as activity

counts per day. Total and physical activity energy expenditure (kcal/day) will be calculated using validated equations.[114,115] Threshold values from a validation study will be used to calculate time spent in sedentary, light, moderate, and vigorous activity. Accelerometer use will be supplemented with a short physical activity log that collects physical activities and time of accelerometer use (hours/day).

Energy Intake

We will obtain detailed data on foods and nutrients associated with energy balance and weight management from total dietary intakes (foods, beverages and snacks): energy intakes, energy density, macronutrient intakes, added sugars, as well as consumption of specific foods and food groups that are excessively high (Sugary Sweetened Beverages, desserts) or inadequate (fruits, vegetables, milk and dairy products, whole grains and fiber) in the typical diets of U.S. children. It is understood that accurate assessment of dietary intakes of free-living individuals is a challenging process and there is no single method that is without limitations. To optimize the accuracy of the assessment of dietary intake data, we will conduct 24-hour dietary recalls using the USDA multi-pass method administered by trained diet recall technicians. Recalls will be performed to capture the average of dietary intakes from 2 nonconsecutive week days and 1 weekend day during the 14-day period of each main study time-point. Diet recall will occur via three phone sessions conducted by the two master trainers at the University of North Carolina (UNC) at Chapel Hill over a maximum of a 30-day period to collect complete participant information. All master trainers will participate in a central in-person training organized by the Research Coordinating Unit (RCU) located at UNC. No diet recalls will be conducted until after the trainer has been trained and certified. Parents will report on themselves and on their child. Analyses will not include data that indicates unrealistically low (eg, <600kcal/d) or high intakes (eg, >4000kcal/d). Dietary data will be entered and analyzed using our NDS-R software (Nutrient Data System for Research, St. Paul, MN). Added sugars will be calculated using the USDA database http://www.ars.usda.gov/Services/docs.htm?docid=12107)z

Study Questionnaire

The study questionnaire will measure a variety of domains and will be provided in both English and Spanish ***(see appendix K for survey)***. It will be a computer-administered questionnaire competed by parents with paper and pencil questionnaire as back-up. ***See Table 1: Collection of Moderators & Mediators for details***. Survey takes about 30-45 minutes to complete.

Metro Parks Staff Questionnaire on Preschool Programs

This survey will assess programs that promote healthy lifestyle activities for both English and Spanish speaking families with preschool age children (3-5 years) in the 22 Nashville Metropolitan Community Recreation Centers. Healthy lifestyle programming includes programs or events that encourage good nutrition and/or physical activity. In addition to healthy program availability, this survey will assess the presence of teaching kitchens in each facility, whereby instructors lead sessions to teach families how to prepare healthy and affordable meals. Participants for this survey are the 22 facility coordinators at each recreation center. The survey will be administered annually online through email via REDCap and is expected to take 10-15 minutes to complete. Since all 22 facility coordinator's (directors) emails are publicly available, we will actively recruit these metro parks staff via email and include a script consenting for their participation to this online survey ***(see appendix R for script)***. Results of this survey aim to

describe the presence and frequency over time of healthy lifestyle programs specifically dedicated to parents and their children at each community center ***(see appendix Q)***. A waiver of consent documentation form (Form #1112) has been completed for the Metro Parks staff who will be consented only before they complete the survey.

Social Networks

We will collect social network data, exploring the potential development of new social ties that could result due to the structure of the study ***(see appendix L).***

Patient Activation Survey

The Patient Activation Measure (PAM) Survey will also be used to determine if obesity-related behaviors (i.e., physical activity, willingness to actively manage one's own health, weight loss) can spread through new social relationships (see attached for survey).The Patient Activation Measure (PAM) is a 13-item measure that assesses patient knowledge, skill, and confidence for self-management.[98] The measure was developed using the Rasch analyses and is an interval level, unidimensional, Guttman-like measure. Reliability and validity was assessed by Hibbard et al., with the 13-item measure. Psychometric properties included scores from 38.6 to 53.0.[98] This survey takes about 5-10 minutes to complete and will be administered at T5, and T6 data collection sessions. Prior to administering this survey, an additional informed consent form will be obtained.

Genetics/Epigenetics

Saliva will be collected from the parent-child dyad participating in the study[116]. For adults, saliva will be obtained utilizing the Oragene saliva kit, collecting 2-3 cc of saliva per participant. For young children, saliva will be obtained utilizing the "baby brush" approach, in which small sponges attached to plastic handles are inserted between cheek and gumline to absorb saliva. Subsequently, the sponges (x4) are cut and placed in the spittoon with DNA preservation solution. We will then use a modification of the Puregene DNA (Gentra, Inc) Purification Protocol for 4 ml Saliva Samples[116], consisting of 4 stages: (1) cell lysis and adddition of RNase to remove RNA from the salivary nucleic acid; (2) DNA precipitation in 100% isopropanol, with 70% ethanol wash; (3) DNA hydration in reduced TE (Tris EDTA) to approximate concentration of 200 ng/u; (4) DNA storage at 4C for working stock, and -80C for archival DNA samples.

Pregnancy Sub-Cohort (GROW Baby)

These data will be collected in two forms: 1) a phone survey; and 2) data from chart reviews, using previously validated abstraction forms for both pregnancy characteristics and infant growth. The phone survey will include questions related to maternal feeding practices between the child's third and fourth month of life. We will use the Vanderbilt Survey Research Core to administer the survey via phone. The survey will consist of 24 items and will assess both parental beliefs and practices about feeding in the first six months of life (see survey attached). The survey will be administered when the child is between 3-4 months of age to identify feeding practices when rapid weight gain can be most detrimental and to minimize recall bias. Because it is a mediator and not a primary outcome, we will only conduct the survey at one point in time to minimize participant burden. This phone survey will take approximately 10-15 minutes to complete.

To obtain chart reviews and records, research staff will request medical records via secure fax from prenatal care, hospital delivery, and nursery records. All chart abstractors will be blinded to study condition (i.e., intervention or control group). A chart abstraction methodology has previously been developed to calculate maternal gestational weight gain. We will abstract data from obstetrical records to obtain at least three additional pregnancy weights, allowing us to use a slope-as-outcome approach, maximizing our power to detect a clinically meaningful difference. Specifically, we will obtain information on height, weight, any medical conditions, and medications they may have taken while pregnant, all of which are typically available in their existing medical record. To evaluate rapid infant weight gain, we will obtain medical records from the hospital delivery records for birth weight and from pediatricians' offices for height and weight measurements through the infants first six months of life.

Family Functioning

Family functioning will be assessed by collecting both: 1) the Family Adaptability and Cohesion Evaluation Scale (FACES IV), and 2) household social network relationships. The FACES IV is a 62 item scale that assesses family cohesion and flexibility dimensions, family satisfaction and family communication styles. There is significant support for the reliability and validity of the scale and it has been used to assess family functioning in almost 500 published studies. Coefficient alphas for all scales range from .77 to .89, with the cohesion and flexibility scales being .89 and .84.[61,117,118] The two balanced scales, cohesion (7 items) and flexibility (7 items) assess the emotional bonding between family members and the quality and expression of family roles and organization, respectively.[61] The additional 4 unbalanced scales asses high and low extremes of family cohesion (disengaged and enmeshment) and flexibility (rigid and chaotic). Respondents are asked to respond to each question on a 5- point Likert scale ranging from (1) strongly disagree to (5) strongly agree. The FACES IV scale has been translated into Spanish and found to be reliable and valid in Spanish speaking populations.[119] The FACES IV will be completed by all consenting household members.

Household Social Network Relationships

Social ties between the GROW parent-child pair, and other participating household family members will be operationalized as multiple relationships (e.g. familial, friendship, cohabitation). Size and composition of family network will be assessed. The strength of the relationship ties will be determined through the FACES IV scales described above. Family Environmental Factors are collected via survey that is delivered in the parent's language of choice verbally (to account for low literacy populations) and directly entered a REDCap survey data base. Additional data that will be utilized to characterize family environment and are already collected as part of the GROW trial.

Qualitative Semi-Structured Interviews

At the study's final data collection, we will conduct a 30-45 minutes semi-structured interview with GROW intervention families to identify how specific behavioral intervention strategies led to

changes in family environment and young siblings' health behaviors (see attached). Our initial sample will include 50 families. Should we fail to reach theme saturation with this sample, we will conduct additional interviews until no new themes emerge. Research assistants will be trained to code on the three initial transcripts, and certified to work once they meet criteria for reliable and valid use of the coding system. Twenty-five percent of the transcripts will be coded twice, with coders kept blind to which transcripts are being used to assess reliability. Coding discrepancies will be reviewed by the coding team, and feedback used to improve the use of the coding system. Interviews conducted in Spanish will be translated and transcribed into English. Interviewers will also collect field notes during the interviews.

Barriers to Physical Activity Questionnaire

This study survey is based from the *Environmental Supports for Physical Activity Questionnaire*[120] to assess individual perceptions of physical activity supports in the social and physical environment, use of the built environment, current physical activity behavior and recreation center use. This survey will take about 15-20 minutes to complete and has been validated in previous literature.[121] These data will help describe the policy environment of study participants and identify policies that enable or constrain active living for participants. The objective of this survey is to link current behavior with local community policies. Specifically, to determine specific neighborhood characteristics that enable or constrain participant ability to be physically active, match participant responses to one of the three policy types: personal safety, transportation, and land use, describe local and state policies that address participant responses, and identify untapped policy options for improving physical activity levels in participant communities. **Geographical Information Systems (GIS):** Using data obtained from external public sources, e.g. data from the Metropolitan Planning Department, the research team will track and map six key measures of active living over the course of the study, such as the ratio of sidewalks to road mileage. These data will be compared to the subjective survey data (i.e., Barriers to Physical Activity Questionnaire – see above) obtained from participants. GIS spatial analysis will use participant addresses to determine correlations between proximity to specific features of the built environment (i.e., data from Metro Planning Dept) and participant data of their perceived built environment (i.e., Barriers to Physical Activity Questionnaire). In addition, these data will also be correlated with local policies (i.e., external data) that support activity living and recreational use and tracked over the duration of the study.

A research team member will conduct an environmental audit of those geo-coded regions from where most of the study participants derive. This will include: 1) block audits where a study team member verifies the existence of built environment elements such as grocery stores, fast food establishments, and corner stores; and 2) utilization of the Nutrition Environment Measures Survey in Stores (NEM-S) to assess the availability and affordability of food/drink in food stores. Similar to tracking key measures of active living, GIS spatial analysis will use participant addresses to determine correlations between proximity to specific features of the food built environment (i.e., environmental audit) and participant data of their perceived food built environment (i.e., NEM-S). In addition, these data will be correlated with local policies that support healthy availability and affordability of food, and tracked over the duration of the study.

Control Measures

The study will use Stephanie Carlson's Executive Function Scale for Preschoolers to determine a comprehensive measure of executive functioning in the child participants of the study. The

battery of hands-on tasks (e.g. card sorting) will be administered by a trained data collector one-on-one to each child and is estimated to take approximately 10 minutes. To measure intelligence of the child participants, the research team will use the Woodcock-Johnson III Tests of Cognitive Abilities – Brief Battery. This tool involves a battery of tasks where children expressively (verbally and/or through pointing) respond to an assortment of pictures and words in a flipbook. Trained data collectors will administer this test individually with each child. The brief battery is estimated to take between 15 and 20 minutes to administer.

Incentives

Data Collection Incentives

After each data collection session, participating families will receive gift cards of varying amounts throughout the duration of the 3-year trial. At times 1, 2, and 4 participants will receive $40. At time point 5, participants will receive $50. Also at baseline data collection, families will receive a small token of appreciation (value of < $10). At time point 3, participants will receive $15 gift card. On the final data collection time (T6), participants will receive $100. For those participants that participate in an additional data collection, one year later (T7), participants will receive a $20 gift card. See Table 2 below for more details.

In order to maintain the integrity of the research, Quality Control (QC) measures will be conducted to ensure the accuracy of data collection. Specifically, research staff will be trained to incorporate one or more secondary measures (i.e., repeat the anthropometric measurements) that can be used to verify the quality of information being collected from the participant. For this trial, QC measures will be collected with random participants at all data collection points. However, due to the additional time and participant burden of these QC checks, an additional $10 gift card will be given to participants (i.e., one per parent and child dyad) to compensate for their time. All QC checks will be conducted by a certified Master Data Collector. These additional measures will take approximately 15-20 minutes to complete.

Table 2: Data Collection Incentives

Data Collection Point	Amount	When
T1 (Baseline)	$40.00*	Half the day of data collection, half on pick up day
T2 (3-months)	$40.00	Immediately after
T3 (9-months)	$15.00	Immediately after
T4 (12-months)	$40.00*	Half the day of data collection, half on pick up day
T5 (24-months)	$50.00*	$20 the day of data collection, $20 after completing child accelerometry and at least 2 out of the 3 diet recalls, and $10 for parent accelerometry and completing the third diet recall.
T6 (36-months)	$100.00**	$25 the day of data collection A, $25 the day of data collection B, $25 for completing child accelerometry and at least 2 out of the 3 diet recalls, and $25 for completing parent accelerometry and the third diet recall.
T7 (48-months)	$20.00	Immediately after

*Participant will receive half of the incentive upfront prior to wearing the activity monitor and the other half upon its return and completion of at least 2 of the 3 diet recalls. Because the 2nd half of the incentive is given only after the wearing of the activity monitor and completing 2 of the 3 recalls, we will arrange a day for the participant to pick up their gift card in person at the community center or we will send it via the US Postal Service.

**Because the 3rd part of the incentive is only given after the wearing of the activity monitor and completing 3 of the recalls, we will arrange a day for the participant to pick up their gift card in person at the community center or we will send it via the US Postal Service.

Intervention Incentives

Intensive Phase: Participants will receive tangible tools or small giveaways during each session. The value of these items will be approximately $3.50 per parent and child dyad each week when sessions occur. Examples of tangible tools, items to reinforce lessons learned are kitchen ware utensils, measuring spoons, etc. In addition to the tangible tools, in order to encourage attendance during the intensive phase of the intervention (weekly for 3-months), participants will have an opportunity to enter a raffle. These raffles will be held during 2-3 sessions, including items such as hand mixers ($10 value) or mixing bowls ($20 value) The odds of winning the raffle in the intervention group is about 1:15, assuming that on average there are 15 people in attendance each week. Notably, the odds vary based on the number of sessions each person attends individually and the number of attendees in the session. Participants in the GROW study will also be invited to aid recruitment efforts by voluntarily filling out the attached referral form at intervention or control sessions with the names, relationship and contact information of other families they may know with a child age 3 to 5. These referred families would be contacted and invited to participate in the study by research staff either by phone or in person. For every family referred who participates in a screening conversation, the participant would receive a small token gift of appreciation valued at $5 (e.g., cooking utensils, key chain, Band-Aid holder, etc.). For every family referred that has met eligibility and are successfully enrolled in the study, the referring participant would receive a $10 gift card as a small token of our appreciation. Word-of-mouth recruitment has been an effective recruitment strategy in our formative phase work. Including small incentives for participants that successfully enroll other interested and eligible families, would serve as an additional strategy to assist recruitment efforts with our hard-to-reach target populations. The maximum number of gift cards participants will receive for this would not exceed $100 over the course of the 3-year trial.

Maintenance Phase: Participants will receive a coupon for a free fitness class of their choice valid at either community center location each month that coaching calls are completed (monthly for 9-months). Fitness classes such as zumba, line dancing, or yoga, etc are routine services offered to the general public at each of the community recreational centers. The value of this coupon is $2.00. Participants that complete all 9-monthly phone coaching calls during the maintenance phase will receive a value of $18 worth of fitness classes for 9-months.

Maintenance and Sustainability Phase: Participants will be invited to participate in classes and various community center events throughout the duration of the maintenance and sustainability phases. Apart from the fitness classes, which are offered by the community centers, we will offer GROW-related community events that focus on nutrition and/or physical activity with parents and children once per month throughout the duration of the 3-year trial. For each class or event attended, participants will receive one punch on their punch card. After every 6 punches, participants will redeem the punch card for a gift valued at $5.00. These small gifts will include kitchen gadgets such as an apple corer, spatula set, wooden spoon set, etc. If participants attended every event during the 3-year trial, participants will have 5 opportunities for a gift valued at $5.00, resulting in a total amount of $25 worth of small gifts in 33-months (maintenance and sustainability phases). For both intervention and control groups, these additional incentives should not pose or be considered coercive since families had already consented to participate in the study. All incentives are tied specifically to participation within the trial and were recommended by families in our prior work in the GROW Formative Phase (IRB No: 100591).

Health-related Incentives

In addition to these incentives, all participants from both intervention and control groups in the study will receive family memberships to their respective community recreational center for one year, which allow adults to use the weight room for no cost. These family memberships will be given to all intervention families during the study and all control families at the end of the study. Moreover, if families use the facility at least once per month, then their family membership will be extended year by year up to 3-years. This will encourage families to utilize their built environment for family physical activity.

The value of the parent and child gym membership for one year equates to $400 at each community center. Although this may be interpreted as undue inducement for families to participate in a 3-year RCT study, providing gym membership to participants allows increased physical activity and healthy living - a direct benefit and positive health advantage to subject participants and their families as opposed to compensation of monetary or economic gains. Since increasing physical activity is directly related to the outcome of the study, we conceptualize offering gym memberships as a bonus and a justified benefit for those that have participated. Compensation will also be given to families participating in the additional sub-cohorts for this research study. For the GROW Baby sub-cohort, participating women will receive a small incentive valued at $20 as a token of our appreciation.
For the ACTIVATE sub-cohort, each parent participant will receive a gift card valued at $10 for completing the PAM and Social Network Survey at each data collection point (a total of 2 data collection points). For all families participating at our data collection sessions, we will provide a nutritious snack.

Randomization

Randomization Schedule

An identical randomization procedure will be followed for each of the three successive cohorts. Available software (e.g., SAS, Stata) will be used to generate a blocked randomization schedule per each strata, within both regions, resulting in 4 total schedules (2 language conditions x 2 regions = 4). Block size will be randomly permuted with the software procedure (although no larger than 10), thereby insuring equal representation at intermittent recruitment points while minimizing the probability of correctly guessing subsequent condition assignment.

Each schedule will be identified by stratum and loaded into the recruitment database. The database security settings will be specified so that once loaded no one on the study team will have write privileges for the schedules, and only the statistician will have read privileges. These settings will prevent anticipation (except for the statistician) or subversion of the randomization process by any member of the study team.

Random Assignment

Each potential dyad's contact information, including child age and dominant language use, will be loaded into the recruitment database upon identification as a potential participant and assigned a unique study identification number (family id). The recruitment database will follow each potential dyad from the point of identification through eligibility assessment and enrollment

through disqualification or randomization. The recruitment database will track all eligibility and enrollment criteria and include a utility that checks still-eligible study candidates for criteria that must be met prior to randomization. Upon identifying dyads who have met all of these criteria, recruitment staff will engage a database utility that performs randomization by identifying the stratum into which each potential dyad should be randomized, and populating the next available slot in the appropriate randomization schedule with the dyad's family id. The database user will not be able to see, and will be unlikely to anticipate, the arm assignment (treatment versus control) for each dyad, especially when multiple dyads within a stratum are randomized at once. Once the dyad is assigned to an arm, a link is established between family id and arm assignment (treatment versus control). This link will not be writable by any study staff and will be viewable by the study statistician in the randomization schedules. Dyad's assignments will be viewable by all study staff on a case by case basis so that the daily activities of managing participants, both parents and their children, may be done without hindrance.

Randomization Data Management

The link between family id and arm assignment will be stored in the randomization schedule, to which only the statistician will have read access. All randomized dyads will remain in the recruitment database for the duration of the study so that recruitment and enrollment reports can be generated on demand by all study staff. By viewing a dyad's record, any study staff can view but not edit the dyad's arm assignment.

All dyads' family ids will be exported into a measurement database along with the fields necessary to conduct timely data collection and on-demand reporting by any study staff. Arm assignment will not be exported to the measurement database. As such, it will not be possible for measurement staff to know a dyads's arm assignment based on the information available in the measurement database.

In addition, once randomized, the family ids (both treatment and control) will be exported into an intervention database along with the fields necessary to conduct the treatment and control procedures and allow on-demand reporting. Arm assignment will not be exported to the intervention database, although its value is implicitly known. As such, intervention staff (in both the control and treatment conditions) will know which dyads have been assigned to which arm, but this knowledge is unavoidable and redundant with knowledge that will be apparent from contact with the dyads within each arm.

Randomization Data Safety

All databases (recruitment, measurement, etc.), will be stored within a password protected shared drive within the university computer system. All study staff will have access to the databases upon submitting the required password. Access to tables within these databases will be made available as needed to perform job responsibilities and in accordance with COPTR policies. The randomization schedule will not be stored in the intervention database making it impossible to access in this manner.

Risk/Benefit Analysis

There are minimal research related risks associated with this study. For this study, suggested exercises will be mild and are unlikely to cause injury. All suggested dietary changes are evidence-based and healthy. If any physical injury or illness should occur as a direct result of participation in this study, VUMC maintains limited research insurance coverage for the usual

and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. The informed consent document will include this statement and will provide pertinent contact information.

The risks to subjects of the study are reasonable, given their minimal nature (e.g., suggested low-moderate physical activity options and healthy dietary changes; learning how to engage their children in dialogue) and given the safeguards employed, as described above. In contrast, we expect tangible benefits to accrue to all subjects of the study: intervention group participants are expected to experience improved healthy lifestyle habits and health outcomes as a result of participating in the study; control group parents are expected to experience empowerment in their ability to prepare their child for school and control group children are expected to be better prepared for school as a result of participating in the study. Also all participants are expected to experience increased parent-child bonding as a result of participating in the study. All participants will receive family memberships to their respective community recreational center, depending on which condition will be during or after study implementation, which allow adults to use the weight room for no cost.

Data Safety and Monitoring Plan

General Description
Comprehensive measures will be implemented to maintain subject confidentiality as appropriate. Study ID number will identify all data collection materials for the study. Only study team members will have access to master linkup lists that match participant names to these Study ID numbers. The master link-up list linking names and Study ID numbers will also contain some basic demographics to be collected for purposes of the study (e.g., gender, maternal education) and personal health information (weight, height, body composition). All data collection forms will be housed at VUMC.

All study data will be kept at VUMC securely locked in a storage area for this study. All data will be obtained specifically for research purposes. The study investigators reviewing the data will not be provided with any participant identification information. Study data collection forms will be maintained under lock and key for 10 years following completion of the study. Thereafter, they will be destroyed. All electronic data files will be stored on a password protected, secure, encrypted server. Only key study personnel will have access to the password. Ten years after study completion, electronic copies of all datasets will be destroyed. Individuals will not be identified in any publications of the study findings.

Data Safety and Monitoring Plan
Purpose: The Data and Safety Monitoring Plan is written to ensure the safety of the participants and to verify the validity and integrity of the data.

Assessment: Participants will be assessed for adverse events at the time of enrollment and when the data is collected at each time-point. The Principal Investigator, co-investigators, study coordinator, intervention lists and all members of the research staff are responsible for the assessment and reporting of adverse events. All spontaneous reports by subjects, observations by clinical research staff, and reports to research staff by family or health care providers will be investigated. The investigators will assess the relationship of the adverse event as not related, possibly related or definitely related using standard criteria for clinical trials.

Possible (to qualify, the adverse event must meet 2 of the following conditions):

1) has a reasonable temporal relationship to the intervention,
2) could not readily have been produced by the subject's clinical state,
3) could not readily have been due to environmental or other interventions,
4) follows a known pattern of response to intervention,
5) disappears or decreases with reduction in cessation of intervention.

Probable (to qualify, the adverse event must meet 3 of the following conditions):

1) has a reasonable temporal relationship to the intervention,
2) could not readily have been produced by the subject's clinical state,
3) could not readily have been due to environmental or other interventions,
4) follows a known pattern of response to intervention,
5) disappears or decreases with reduction in cessation of intervention.

Definite (to qualify, the adverse event must meet at least 4 of the following conditions):

1) has a reasonable temporal relationship to the intervention,
2) could not readily have been produced by the subject's clinical state,
3) could not readily have been due to environmental or other interventions,
4) follows a known pattern of response to intervention,
5) disappears or decreases with reduction in cessation of intervention.

Policy for Blinding in COPTR

January 26, 2012
Revised July 24, 2014

Introduction

In all clinical trials, the potential for bias is one of the main concerns. Bias arises from conscious or subconscious factors, and can occur from the initial design through study conduct, data management, data analysis and interpretation. A general approach to avoid biases is to keep the participants and the investigators blinded to the identity of the assigned arms until all data points are collected. As stated by Friedman, Furberg and DeMets, a fundamental point is that: "*A clinical trial should, ideally, have a double-blind design in order to avoid potential problems of bias during data collection and assessment. In studies where such a design is impossible, other measures to reduce potential bias are advocated*."

Guiding principle #1: All COPTR personnel that are in a position to change the study protocol or its implementation in study participants, should be blinded to information that may allow them to do so, from when the study starts until the study ends, with specific exceptions as delineated in this document.

Clarification of terms:

- The "study starts" at a site when the first participant is randomized.
- The "study ends" at a site when the outcomes (primary and secondary) of importance to the site have been collected on all participants.
- "Interim' information is information that is collected between the study start and the study end at a given site.

As stated in the "Decision Making Protocol," there are Common and Site-specific elements:

- **Common elements** refer to those measures that two or more sites collect, protocols and manual of procedures related to those measures, and reporting processes.
- **Site-specific elements** refer to those measures and operational activities that relate to only one site.

With respect to study information/data, the following is to clarify terms:

- Study data – any information collected on study participants, which includes
  - Primary and secondary outcome variables
  - Demographic variables
  - Mediators and moderators
- Outcome variables – primary and secondary outcomes as described in site protocols
- Process variables – e.g. training, recruitment, intervention implementation, fidelity, adherence, retention/attrition

Also, data are available at multiple levels:

- Individual subject level, including subject's family or community
- Aggregated by arm, that is, collapsed from individual subject level and combined or averaged by study arm

Guiding principle #2: All COPTR study site personnel (staff and investigators) should be blinded to study data aggregated by study arm that have the potential to impact the study's outcome, or if not possible, measures need to be taken to reduce potential bias. Specific exceptions are delineated in this document.

Study data 'that have the potential to impact the study's outcome include aggregated: arm-level outcome variables, mediators, moderators (OMM), and process variables. Individual level outcome variables, mediators, moderators, process, and demographic variables are not blinded. Arm-level demographic variables are not blinded.

There may be specific process data collected in one or more arms that the Principal Investigator and study staff want to review aggregated by arm before the end of the study. Those variables will be declared *a priori* by each site, reviewed by the Design and Analysis Working Group, and approved by the PI. Those variables will be clearly listed as unblinded variables in the final study protocol. Should sites wish to examine additional blinded process variables aggregated by arm, after the study has begun, those requests would also be reviewed by the Design and Analysis Working group and, if access is approved by the PI and by the DSMB, those variables will be clearly listed as unblinded variables in an amendment to the study protocol. Subsequent references in this document to process data will distinguish between blinded and unblinded process variables.

In clinical trials that require **interim** monitoring, it is an accepted principle that interim OMM and blinded process data aggregated by arm should be kept confidential, with such data accessible only to a small number of individuals responsible for its analysis and monitoring. Generally, blinding to intervention arms should be maintained to the extent possible until the study ends. In COPTR, study investigators and sponsors are not privy to interim OMM and blinded process data aggregated by arm, and only the study or independent statisticians/analysts preparing and presenting the analysis to the DSMB, as well as the DSMB, are unblinded.

The study arms in the 4 trials are, BY DESIGN, not able to be totally blinded. However, some blinding can be maintained. Measurement staff should not be informed of the intervention that individual participants are receiving, and should have **no role** in the delivery of the intervention. Efforts should be made to avoid participant (child/parents) interactions that result in open chatting with assessors about the interventions they have received. Measurement staff should be trained to end any such communication when initiated by participants.

Study investigators and staff are kept blinded as to the ARM level results until study end. That is, they should **never** see or hear OMM and blinded process data aggregated by arms until the DSMB allows it. Exceptions to this policy are made only for individuals and circumstances in which unblinding is necessary for the preparation of reports to the DSMB. Ancillary studies need to adhere to these same principles.

Table 3. Summary of issues related to maintaining objectivity as applied to COPTR

	COPTR
Interventions are comparable and suitable for blinding	**NO, BY DESIGN**
Investigators/staff are blinded as to arm of an **individual** participant	**NOT POSSIBLE**
Individual child and/or parent participants are blinded as to the intervention they are receiving	**NOT POSSIBLE**
Outcome assessors are blinded as to the intervention the **individual** participant is receiving	**YES**
Site investigators and all study staff, except site statisticians/analysts, are blinded as to ALL the aggregated by arm interim OMM and blinded process data	**YES**
Site Statisticians/analysts at each field site are blinded as to the aggregated by arm interim OMM data on **common** measures	**YES**
Site Statisticians/analysts at each field site are blinded as to the aggregated by arm interim OMM on **site-specific** measures	**NO**
Site staff are unblinded to the aggregated by arm process measures identified *a priori* or by amendment to the protocol as unblinded	**YES**

Guiding principle #3: In COPTR, the RCU will function as the 'Independent Statistician,' while the individual study center statisticians/analysts will function as the 'Site Statistician.'

The rationale for keeping investigators and sponsors blinded to interim data is generally accepted. The possible conflict of interest that could arise for the site statistician or analyst who performs the analysis of the interim data and presents it to a data monitoring committee has received little attention. Ellenberg and George (2004) describe some potential conflicts for the Site Statistician, and approaches that might be taken to minimize them.

Ellenberg & George (2004) argue that a reason for not blinding the Site Statistician is the assumption that the Site Statistician is someone "with no obvious intellectual conflicts of interest who, by training and temperament, can be trusted to provide a dispassionate analysis of the accumulating data." This objectivity assumption may or may not be true, and there are many pressures exerted on the Site Statistician that is employed and part of the team at a study site.

Each of the 4 COPTR sites has identified an individual(s) who will serve as the Site Statistician. The **Site Statistician is the person(s) responsible and accountable** for maintaining the blind of any site-specific study OMM and blinded process data from all other site study investigators and staff. It is the responsibility of the site Principal Investigator to ensure that the Site Statistician understands his/her role and responsibilities. The Site Statistician must have no communication with others at the site, formally or informally, about trends in OMM and blinded process data and side effects. They must also safeguard data files, printed output, log files and any emails or correspondence related to the OMM and blinded process data and side effects with the RCU and the DSMB. It is their responsibility to take care in destroying printouts and correspondence – ideally by shredding. It is also their responsibility to make sure that any discussion and communications of blinded data with the RCU and DSMB are confidential.

The Site Statistician:

iv. will be blinded to aggregate comparisons by arm of post-randomization COMMON OMM data until all endpoint data have been collected at their site unless otherwise instructed by the DSMB.
v. will remain objective when carrying out the activities of conducting the trials – preparing randomization schemes, randomizing individual subjects, processing of the data, cleaning and editing the data, preparation of analyses/reports of site-specific OMM and blinded process data, and transmitting the COMMON OMM data to the RCU; and
vi. is responsible and accountable for maintaining the blind of study site investigators and staff at their site with respect to OMM and blinded process data aggregated by arm.

The RCU:

v. is the only entity that has personnel that are unblinded to the COMMON OMM data aggregated by arm during the trial;
vi. will prepare analyses/reports to the DSMB of the COMMON OMM data and adverse events aggregated by arm, as requested by the DSMB;
vii. shares responsibility for maintaining the blind of study site investigators and staff; and
viii. is responsible and accountable for maintaining the blind of co-investigators from NIH and RCU staff who do not need to be unblinded with respect to COMMON OMM data aggregated by arm in order to complete their duties.

Responsibilities of the Site Statistician and the RCU

It is imperative that professional ethical conduct guidelines be followed by the Site Statistician and the RCU Independent Statisticians at each stage of the study. The Site Statistician prepares the randomization scheme and thus handles the list (datafile, database table, etc.) linking study ID to assignment that permits looking at the data aggregated by arm. Thus, this person(s) must exercise care in protecting the treatment allocation list and ensuring no one – including him/herself - conducts any analyses of COMMON OMM variables, adverse event or other follow-up information aggregated by arm. The Site Statistician may prepare descriptive reports of site-specific data aggregated by study arm if so directed by the DSMB or RCU. All study data must be protected in secure, password protected files or databases with only the Site Statistician, their programming staff, and the RCU having access to the data files. Note that data needed to interact with and track families (e.g., names, ages, contact info, etc), will not be blinded to interventionists, of course.

The list (datafile, database table, etc.) created by the Site Statistician that contains the subject ID and the allocation to study arm is protected in a secure and password protected manner with only the Site Statistician and the RCU having access to the information.

Blinding of Investigators by Data Type

All data collected will be categorized *a priori* into one of 7 categories:

viii. *Demographic* information, such as age, sex, country of origin, and contact information is not blinded, either at the individual level or aggregated by arm.

ix. *Study arm assignment* is concealed until the time of randomization.

x. Post-randomization, all field center or site personnel are blinded to *common OMM data, aggregated by arm*, except as allowed by the DSMB.

xi. Post-randomization, all site personnel except the site statisticians/analyst are blinded to site-specific OMM data, aggregated by arm. The site-specific OMM data, aggregated by arm, are held strictly confidential by the Site Statistician, programmers they designate, and the RCU as detailed in this document.

xii. *Post-randomization, individual level process data* are viewed by the Principal Investigators throughout the study and may also be shared with the interventionists, Project Coordinator or Manager. *Arm-level process data* may be viewed by the Principal Investigators and shared with the interventionists, Project Coordinator or Manager, if those variables are first reviewed by the Design and Analysis Working Group, approved for access by the PI, and listed *a priori* as unblinded variables in the study protocol or as an amendment to the study protocol.

xiii. Post-randomization, blinded process data, aggregated by arm, are held strictly confidential by the Site Statistician, programmers they designate, and the RCU as detailed in this document.

xiv. *Safety data* are collected for the purpose of insuring participant safety. Guidelines for viewing these data have been designed by the COPTR Subcommittee on Recruitment, Retention, Consent, Adverse Events and Safety.

Blinding of Investigators to Study Data by Study Stage

iv. **All** *baseline data* from an individual subject are collected prior to allocation to a study arm. Following all baseline data collection on an individual subject, allocation information on that subject is made available to site study staff as needed. Comparative baseline (pre-randomization) data may be viewed by investigators and study staff in aggregate by arm (e.g., for reporting comparability of groups in a design and/or baseline manuscripts). The site investigators may analyze and publish data collected at baseline using the usual policies of subject confidentiality and protection and guidelines set by the COPTR Subcommittee on Publications, Presentations and Ancillary Studies.

v. *Interim Data (post-randomization)*. All analysis of post-randomization data is required to have discussion and approval by PPA, D&A, the Steering Committee, and the DSMB, with the exception of analyses conducted by the RCU for purpose of completing the DSMB report and pre-approved analyses of process-level data. All site personnel are blinded to *common OMM data, aggregated by arm*, except as allowed by the DSMB. All site personnel except the site statisticians/analyst are blinded to site-specific OMM data, aggregated by arm. The site-specific OMM data, aggregated by arm, are held strictly confidential by the Site Statistician, programmers they designate, and the RCU as detailed in this document. *Individual level process data* are viewed by the Principal Investigators throughout the study and may also be shared with the interventionists, Project Coordinator or Manager. *Arm-level process data* may be viewed by the Principal Investigators and shared with the interventionists, Project Coordinator or Manager, if those variables are first reviewed by the Design and Analysis Working Group, approved for access by the PI, and listed *a priori* as unblinded variables in the study protocol or as an amendment to the study protocol. Blinded process data, aggregated by arm, are held strictly confidential by the Site Statistician, programmers they designate, and the RCU as detailed in this document. **No interim OMM or blinded process data from any arm are available for publication or presentation until the end of the study, unless the plan has been (1) reviewed by the Design and Analysis Working Group and the Publications Subcommittee and (2) approved by the site PI, the Steering Committee, and the DSMB.**

vi. *Final data. Final data* are held private at each site or at the RCU in the same manner as the Interim data until the end of the study. The end of the study at each site is defined as the moment that the last study data point at that site has been collected and recorded. This includes data from all study index children as well as data from other individuals and entities at a study site. At the end of the study, all study data, including data on study arm assignment, can be accessed by study investigators using the usual policies of subject confidentiality and protection and guidelines set by the COPTR Subcommittee on Publications, Presentations and Ancillary Studies.

Preparation of Study Data Reports for the DSMB

v. Accumulated data will be 'frozen' at a specified date for the particular report. A copy of the 'frozen raw datafile of COMMON measures' is sent to the RCU for analysis along with the protected list of the treatment allocation.

vi. After processing, cleaning, editing, creating derived variables, the dated 'analysis files' of COMMON variables (including treatment allocation) and relevant documentation are sent to the RCU. Site-specific data are not sent to the RCU.

vii. For COMMON variables, the Site Statistician conducts analyses for the purposes of data cleaning and looking for outliers, unusual trends and distributional anomalies of the data from their own site, overall – **not** by study arm. They do not generate comparative analyses by study arm. Information generated (not the raw data) may be shared with other site investigator/s for the purposes of conducting data cleaning. The cleaned COMMON variables data are sent to the RCU, along with means and frequencies for all variables. The RCU will prepare means and frequencies for all variables and compare them to the site results to confirm accurate transfer of data. The RCU will prepare descriptive and quality control tables for presentation to the DSMB, both overall and by study arm. No modeling is done by the RCU unless they are specifically instructed to do so by the DSMB.

viii. For **site-specific** data, the Site Statistician conducts analyses for the purposes of data cleaning and looking for outliers, unusual trends and distributional anomalies from their own site, in a manner similar to that described above for COMMON variables. Different from common variables, the Site Statistician prepares descriptive and qualitative data reports using templates developed in cooperation with the RCU. These reports will not be generated by study arm unless instructed to do so by the DSMB. Otherwise, site-specific variables will be examined only with data from all study arms combined.

Data on Participant Safety

As with other data, safety data will be blinded, as possible, to the investigators and staff at each site (not possible when obviously related to the intervention or collected during an intervention activity, for example). The objectively collected adverse events data, however, are collected the same way in all arms and will be blinded. Sites should see only aggregate data (all treatment arms combined) although RCU can prepare data for DSMB by arms.

Treatment condition unblinding recommendations

<u>Study arms</u>

Decisions to unblind the site investigators to arm-level experimental assignment will be the responsibility of the DSMB according to the following steps.

vi. RCU prepares adverse events and safety reports by unidentified arm (e.g., group A, group B) in the twice-yearly DSMB reports.

vii. DSMB reviews adverse events and other safety-relevant data at their periodic meetings.

viii. If the DSMB identifies a potentially important difference between arms in adverse events or other safety-related data, they may request additional analyses and/or request unblinding of arm assignment (e.g, treatment and control), and may consult with the NIH, RCU and PI(s) to help them interpret the findings. Unblinding, if necessary, should be limited to only those investigators who need to know to protect the safety of participants.

ix. If the DSMB determines that the differential between arms may impact the safety of participants and/or changes the assessment of risk of participation, they will make the appropriate recommendation to the NIH who, in turn, will notify the site PIs, accordingly.

x. It is the responsibility of the site PIs to report to their site IRBs.

Presentation of Reports to the DSMB

The RCU statisticians will be presenting the report, which includes the report on the common measures, plus each site's site-specific variables report. The Site Statisticians are available to be contacted by phone during the DSMB meeting in case questions arise that they are in a better position to answer about the site-specific variables and the overall site analyses. Site Statisticians may not participate in any portion of the meeting or call in which unblinded common OMM data are discussed.

Timeline for preparation of reports to the DSMB

Typically there is a roughly a 7-week period prior to the date of the meeting for preparing the DSMB report. Adherence to this timeline assumes that data entry and cleaning have been ongoing and that templates used to generate tables have already been created. It also recognizes that some data, such as blood analyses, actigraph, and diet data, that undergo other processing, may be delayed in comparison to other types of data.

Table 4. Timeline for preparation of reports to the DSMB

-7 weeks	• data 'frozen' for the report on same date at each field site • copy of raw frozen COMMON measures files sent to RCU
-5 weeks	• data processing, data cleaning, data editing, datafile creation at each field site completed • clean COMMON measures files sent to RCU
-3 weeks	• data reports on site-specific variables prepared, reviewed at each field site and sent to RCU • data reports on COMMON variables prepared and reviewed internally at the RCU
-2 weeks	• RCU compiles reports, assembles binders and sends to DSMB
0 weeks	• DSMB meeting

At the meeting, the RCU presents the report, and afterwards collects all reports for archival. The RCU communicates with site investigators and Site Statisticians on relevant issues raised by the DSMB – such communication is not shared with other site staff or investigators.

Communication of the Policy for Blinding in COPTR

In order to insure that this policy is clearly understood and communicated, all COPTR study Principal Investigators, the NIH Project officer, the Site Statistician and the RCU members involved in data management or analysis will confirm compliance. Over the course of the study as new personnel are hired, they will also confirm compliance. This will be done by each of these individuals sending an email to the COPTR Communications Manager as follows:

> I have read, understood and agree to comply with the 9 page document entitled, *Policy for Blinding in COPTR.*

The RCU will maintain a list of the names of individuals from whom this confirmation has been received, and this list will be available for inspection by the DSMB.

References

3. Ellenberg SS, George SL (2004) Should statisticians reporting to data monitoring committees be independent of the trial sponsor and leadership? *Statistics in Medicine* 23:1503–1505.
4. Friedman LM, Furberg CD, DeMets DL (2010) Fundamentals of Clinical Trials, 4th ed., Springer, NY.

Study Design, Statistical Consideration and Analysis Plan

Study Design

The design of the study is a longitudinal non-blinded (open) randomized control trial. Within each of two sites, adult-child dyads with children ages 3-5 years will be randomly assigned, stratified according to parent language use (English or Spanish), to either the three-year prevention program or the control condition. Assessments will occur over six time points within each cohort, beginning at baseline and including assessments post-intervention (at 12 weeks/3 months), and at 9, 12, and 36 months from baseline.

Primary Research Question and Hypothesis

Our primary research question is about the impact of the GROW trial on the growth rate of children's BMI over time. Specifically, we hypothesize the following:

Hypothesis 1: The BMI trajectories of children in the treatment group will change at a slower rate than those in the control group over time.

Primary Outcome

Although childhood obesity is a well-documented public health concern, most studies have assessed the obesity outcome (e.g., BMI) using only a single time point or incorporating a pre-post design, leaving us with little knowledge about the actual shape or growth rate of trajectories of BMI during this critical period of development. Indeed, few studies have taken a developmental perspective in order to understand how and when obesity develops in early childhood. By measuring BMI at multiple time points, we will examine growth trajectories in early childhood. This will allow us to examine the effect of a prevention program on these varying trajectories (Agras, Hammer et al. 2004; Pryor, Tremblay et al. 2011). As Barker et al. demonstrated, it is the change in BMI over time in early childhood, rather than BMI at any one time point, that is linked with health consequences in adulthood (Barker, Osmond et al. 2005). Moreover, an earlier childhood adiposity rebound is associated with an increased risk of later obesity (Rolland-Cachera, Deheeger et al. 1984; Cole 2004). Because clinical literature about childhood obesity indicates that the shape of the BMI trajectory across ages three to eight is curvilinear, we will account for this in our analytic plan (Kuczmarski, Ogden et al. 2002; Cole 2004) (see below).

Primary Analysis

Statistical model and approach

Our primary analysis will be an intent-to-treat analysis, and we will fit a multilevel mixed-effects linear model using a maximum likelihood procedure to handle missing data.

Time-varying BMI will be the outcome at Level 1 nested within children at Level 2. Time at Level 1 will be in years since baseline as computed from the date of each child's measurement at each time point. The following child-level (Level 2), time invariant variables will be predictors of the linear and quadratic BMI growth rates and the intercept at Level 1: age at baseline (centered at a value of interest) and random assignment to intervention or control. Child gender will be a child-level (Level 2), time invariant predictor of the intercept at Level 1. This approach allows the estimation of growth rates based on each child's individual measurement dates, and accounts for both age at baseline and time in the study.

The Level 1 equation is as follows:

$$BMI_{ti} = \pi_{0i} + \pi_{1i}(Time)_{ti} + \pi_{2i}(Time)^2{}_{ti} + e_{ti}$$

where BMI for each child *i* is repeated over time *t*. BMI for a given child is a function of the individually varying baseline intercept π_{0i} , the linear growth rate π_{1i} across 36 months, the quadratic growth rate (acceleration) π_{2i} , and a random error term.

The intercept and two growth parameters will then be regressed on Level 2 (child-level) predictors as follows:

$$\text{BMI Intercept: } \pi_{0i} = \beta_{00} + \beta_{01}(age - C)_i + \beta_{02}(I)_i + \beta_{03}(F)_i + r_{0i}$$

$$\text{Linear Growth: } \pi_{1i} = \beta_{10} + \beta_{11}(age - C)_i + \beta_{12}(I)_i + r_{1i}$$

$$\text{Quadratic Growth: } \pi_{2i} = \beta_{20} + \beta_{21}(age - C)_i + \beta_{22}(I)_i + r_{2i}$$

where *I* is an indicator for group assignment and equals 1 for the intervention group and 0 for the control group, and *F* is an indicator for sex and equals 1 for females and 0 for males. β_{00} is the mean initial BMI in control group males while adjusting for child age at baseline (centered), β_{01} is the effect of child age at baseline (centered) on initial BMI, β_{02} is the effect of being assigned to the intervention group on initial BMI (expected to be 0), β_{03} is the effect of being female on initial BMI, and r_{0i} is the random error variance. β_{10} represents the linear growth rate at baseline in the control group while adjusting for child age at baseline, and β_{11} is the effect of child age at baseline on linear growth. β_{12} is the intervention effect on linear growth, and β_{22} is the intervention effect on BMI acceleration while adjusting for child age at baseline.

The Level 1 and Level 2 equations can then be combined and regrouped to yield a single equation for the model:

$$\begin{aligned} BMI_{ti} = {} & [\beta_{00} + \beta_{01}(age - C)_i + \beta_{02}(I)_i + \beta_{03}(F)_i] \\ & + [\beta_{10}(Time)_{ti} + \beta_{11}(age - C)_i(Time)_{ti} + \boldsymbol{\beta_{12}}(I)_i(Time)_{ti}] \\ & + [\beta_{20}(Time)^2_{ti} + \beta_{21}(age - C)_i(Time)^2_{ti} + \boldsymbol{\beta_{22}}(I)_i(Time)^2_{ti}] \\ & + [r_{0i} + r_{1i}(Time)_{ti} + r_{2i}(Time)^2_{ti} + e_{ti}] \end{aligned}$$

where the terms in the first bracket contribute to the intercept, the second bracket's terms contribute to the linear growth, the third bracket's terms contribute to the quadratic growth, and

the final bracket contains all of the random error terms. We will specify an unstructured variance-covariance matrix.

We will conduct a likelihood ratio test with two degrees of freedom to test whether the linear and quadratic intervention effects (β_{12} and β_{22}, respectively) are jointly equal to zero. If this joint test is not significant at p<0.05 then intervention effectiveness is not demonstrated. If this joint test is significant at the p<0.05 level, then the intervention effect was significant.

Checking and Sensitivity Analyses: Once a model has been estimated, we will need to investigate its properties not only to ensure that any data idiosyncrasies do not impact the results but also to help ensure that the results are generalizable. The first issue is to check for systematic differences between the model and the data using graphs, such as comparisons of predicted and observed values of BMI, and other standard diagnostics (Snijders 2008). An extension of this idea is to simulate new sets of outcomes, based on our model, and use the simulated data as a reference test group by comparing this set to the observed result; in this case, we would look for situations in which the data appear different from what we would expect by using the model to predict the data (Gelman 2007).

A second issue is whether we have left out important features of the model, including, for example, (1) age at randomization, (2) measurement occasion, (3) study wave (by which we mean enrolled in first year, second year, or third year of the program), or (4) other demographic variables (e.g., SES, parent level of education) or substantive covariates (e.g., maternal depression). Some of these variables will be tested explicitly as moderators or mediators (see previous sections pertaining to moderators and mediators as well as sections 11.6 and 11.7 below). In addition, trajectories may vary by baseline BMI; this possibility will be checked by estimating a model with a baseline BMI by treatment group interaction. We will estimate additional models that include one or more of these additional features to check whether inclusion of any of these predictors is both statistically reasonable and affects our conclusions.

A third issue is whether age is correctly specified. With six data points, a limit exists as to what can reasonably be done. We suggest that the quadratic model should be checked in two ways: (1) substitute linear splines with a break between, for example, ages 4 and 5 (anticipated adiposity rebound timing); (2) substitute non-linear splines, in particular, restricted cubic splines with 4 knots chosen following Harrell's default positions (Harrell 2001).

A fourth issue relates to the potential correlation among the clusters/subgroups in our analysis: to what extent are these clusters correlated, what is the effect of that correlation on our results, and how accurately have we specified the clusters? Although we will not use the cluster-adjusted robust sandwich estimator in our primary analysis, we will, as a safeguard, fit a model that assumes a cluster structure within the data and compare the standard errors of this model to those from our primary model. If there are substantive changes in the standard errors, further work will be done to see which set of standard errors is more appropriate in our situation.

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

Estimated Attrition: Within each planned cohort of 200 dyads per three cohorts, six waves of data collection will occur, with shorter time intervals between the earlier waves and longer time intervals later. According to prior community-based studies, subject dropout decelerates over time, with the worst losses occurring early. We will make every effort to reduce attrition, with particular focus on the earlier waves of the study, to ensure that we retain at least 80% of our sample within each cohort, yielding a cohort size of at least 160 and a total sample size, at study end, of at least 480. This level of attrition would leave us sufficiently powered (.90) to be able to detect a standardized effect size of .40 (a respectable and common effect size unique to the analytic method we are using--see sample size and power analysis section). An even larger sample size will increase the power to detect a meaningful difference, as explicated in the power analysis and sample size section below, and we will strive to ensure that the sample is as large as possible at each successive wave. In addition, it is important to note that our analysis is an intention-to-treat analysis. Accordingly, we will use all cases in our analyses, even those with as few as one wave of data, such that attrited cases will not truly be lost but instead retained in our analytic procedures.

Missing Data: Conceptually, we anticipate two types of missing data: (1) people who drop out after a measurement occasion and never return [i.e., lost to follow up]; and (2) people who miss one or more particular measurement occasions (e.g., occasion three) but are present for each of the others, at least one of which is later in time than the one (or more) that they missed.

With six repeated measurements, some participants inevitably will miss one or more occasions of outcome data collection. One advantage of the mixed models over older repeated measure ANOVA models is the use of all available data without dropping any subjects (Nich and Carroll 1997). We begin by assuming that the missing occasions meet MCAR or MAR assumptions (Little and Rubin 2002). If so, the results of the mixed model (e.g., the effect of time, group by time) are robust.

To guard against missingness biasing results, we will also conduct secondary analyses of missingness to see how realistic the assumption of MAR or MCAR may be. This check can be done in several ways. We will start with descriptive statistics comparing the characteristics of observations with and without missing values (e.g., gender, baseline BMI, age at enrollment, etc.). The first analysis will use standard multiple-imputation with 100 imputations (Little and Rubin 2002). Three possible directions, in addition to standard diagnostics (White, Royston et al. 2011) can be pursued when checking whether being missing is non-random (i.e., in checking the results of the multiple imputation):

1) The first method is our primary suggestion: we will impute the data using standard multiple imputation (MI) software but with constraints on the values that can be imputed. These constraints arise because our prime concern regarding non-random missingness is that either those who don't need the program (i.e., those who are lean) or those who perceive that they are not seeing an effect (i.e., who are, and remain, overweight) will miss occasions. For example, in one set of imputations we would constrain all imputed

BMIs to be below, say, “a”; in a different set, we would constrain the imputed BMIs to be above, say, “b”; this type of constrained MI is discussed in An and Little(An, Little et al. 2010) and Jenkins, Burkhauser, Feng, and Larrimore(Jenkins, Burkhauser et al. 2011). One hundred imputations will be used for each such constrained MI. We will examine the BMI pattern of those who drop out and, if we see evidence of either "a" or "b", use the values we observe to set the constraints.

2) A second possible type of sensitivity analysis was originally suggested by Rubin (1987) and has been extended by Carpenter, Kenward, and White,(Carpenter, Kenward et al. 2007) who suggest weighting each imputed result (rather than Rubin's standard simple averaging of the results), where the weight depends on the assumed departure from the MAR assumption. Their technique relies on at least one strong assumption, but they provide a graphical diagnostic to help check this assumption.

3) If drop-outs (situation one above) are much more common than missing an occasion and then returning (situation two above), we will estimate a pattern-mixture model (Little 1993; Hedeker and Gibbons 1997). If missing one or more occasions and then returning is relatively common, however, we will not pursue this strategy.

Detectable Difference, Sample Size, and Power

Power and Sample Size Estimation: The power analysis was performed on our primary analysis (see below): a quadratic model of the BMI trajectories. For our sample size estimation, we used the OD (Spybrook 2011) software so that we would be consistent with our planned analysis. This software allowed us to examine two-group repeated-measures trials with quadratic change, the same model being used for the analysis.

This software uses a standardized effect size as defined in Raudenbush and Liu, namely, the group difference on the polynomial trend divided by the “population standard deviation of the polynomial trend of interest” (p. 391; the “population standard deviation” refers to the square root of the variance of the random effect) (Raudenbush and Xiao-Feng 2001). This specification, particularly the denominator, is quite different from cross-sectional standardized effect sizes such as Cohen’s D, given that, with a polynomial model (here quadratic), the difference between groups depends on the point in time examined. In particular, given our hypothesis (see below), we expect that, after adiposity rebound is reached, the BMI of children in the intervention group will grow more slowly than that of children in the control group such that the differences between their mean BMIs will increase over time**.** Our expectation implies that we are interested in the significance of the quadratic term in the model, and expect that the difference between the control and treatment group quadratic effect will be significantly different from zero.

We note one difference between the OD program's assumptions and our study: the OD program assumes that the measurement occasions will be equally spaced over time, which is not the case in our study. As a result, specifications from the OD program may lead us to overestimate power and underestimate sample size. Power is high in the current study, as can be seen in the table below, thus we expect that these potential mis-estimations are not problematic.

To determine the power and effect size of the current study, we need estimates of the standardized effect size, which we obtained from a subset of our previous Salud Con La Familia study. We used only a subset of the Salud subjects because the inclusion criteria for that study (i.e., children at any level of baseline BMI) were broader than for the current study (i.e., children whose baseline BMI is between the 50th and 95th ([or 99th] percentile). For our estimations, then, we used only the Salud data for those from the 50th to the 95th percentile (and then again from the 50th to the 99th percentile [see below]). Other important differences exist between Salud and the current study, however, that limit our ability to estimate power and sample size based solely on Salud: (1) the Salud subjects had only three measurement occasions which covered 15 months rather than six occasions over three years (the GROW trial) and (2) the Salud intervention was comparable only to the 12-week intensive phase proposed in the GROW study and did not include a maintenance or sustainability phase as proposed in the GROW trial. We expect that the increased number of sessions as well as the intensity of the intervention in the GROW trial will serve only to increase the power of the GROW study.

When using the OD software, the user can set various values, the most important of which is the standardized effect size discussed above. Other possible values to set include the duration of the study (here, three years), the number of measurement occasions (here six), and the variance of the residuals and the variance of the random effects. We found that even fairly sizable changes in value used for the residuals and the variance of the random effects had little effect on the projected sample size (e.g., holding other elements constant and changing the variance of the random effect of age-squared from the observed standard deviation of 2.8 [based on the Salud data] to the OD program's default of 1, only increased the sample size at a power of 0.8 by about 20 subjects). Using the program defaults for residuals and variance of the random effects was a conservative (i.e., produced larger estimates of sample size) approach compared to using the results based on Salud, thus we used these defaults in the table below. Changing the standardized effect size does have important consequences for the estimated sample size, however (see Table 5).

As previously stated, we used the Salud data to estimate our primary model (see below) for those within that study who were between the 50th and 95th BMI percentiles at baseline. The control group in the Salud data showed unexpected results with virtually no non-linearity (i.e., their BMI trajectories increased but in a linear fashion over a 15 month period), therefore we believe that the effect size from that model, which was quite large and based on different assumptions, is an overestimate of the effect that we will see in the GROW study. Instead we used the OD program default for the effect size of 0.4, a commonly used effect size in longitudinal studies and thus the OD program default, to estimate our required sample size. Accordingly, Table 5, below, indicates, for powers of 0.7, 0.8, and 0.9, the estimated sample size using the OD program for the default effect size (0.4) and for two additional effects sizes, a smaller and more conservative effect size (0.3) and a larger and more liberal effect size (0.5). As the table below indicates, we estimate that retaining a sample size of at least 480 will leave us adequately powered to determine this middle/medium effect size of 0.4.

Table 5: Estimated required sample size for given standardized effect sizes

Power/Effect Size	Sample size for Standardized Effect size = 0.3	Sample size for Standardized Effect size = 0.4 *(OD program default)*	Sample size for Standardized Effect size = 0.5
70.00%	500	285	186
80.00%	640	360	232
90.00%	860	480	308

Because the results of our pilot study currently underway have led us to consider including children with higher baseline BMI in the GROW trial than we had originally planned, we also estimated our primary model on Salud participants who were between the 50th and 99th percentile of baseline BMI to determine the effects of including these children with a higher BMI. While, as expected, the variance increased when we moved to the model that added children between the 95th and 99th percentiles, the difference between groups (control and intervention) also increased such that the standardized effect size changed very little and, thus, there was virtually no effect on power (i.e., the desired sample size, under various conditions, never changed by more than two people). If, then, we decide to extend our criteria in the GROW trial to include children who are in the 95th to 99th percentile of BMI at baseline, our analyses will continue to be sufficiently powered.

Currently, the design for the GROW trial includes 600 children, and, though we would expect to be adequately powered at a smaller number of subjects, we plan to recruit 600 subjects to allow for potential attrition. We note, however, that if recruitment of that higher number of subjects becomes problematic (and we have observed in our current pilot study the difficulties inherent in recruitment for a similar prevention trial), we will stop subject recruitment at a smaller number of subjects, though ideally not less than 480 (see Table 5), such that we are adequately powered.

Analysis for Possible Effect Modifiers

The variables that are listed in the previous section as moderators (e.g., race/ethnicity, genetic risk score, etc.) will be entered appropriately into the analytic model as interaction terms in order to test the effect of the moderator on the outcome (child BMI trajectory). Relevant three-way interactions (e.g., child gender by age by group) will also be tested.

Analysis for Possible Effect Mediators

The variables that are listed in the previous section as mediators/covariates will be entered into the analytic model as time-varying covariates and their effects on the outcome will be assessed accordingly, controlling for all else in the model.

Secondary Hypotheses and Analysis

Secondary Analyses: We list below two sets of secondary analyses. The first is specific to our primary analysis (see Aim 1, Hypothesis 1); the second is specific to the secondary aims and related hypotheses (see Aims 2-6) and contained under section 11.9 (below).

Secondary Analyses in relation to the Primary Hypothesis and Analysis

1) Timing of adiposity rebound: We anticipate that we will be able to characterize and capture the timing of adiposity rebound for many of the children enrolled in the study. At time of enrollment, each child is at least three years of age and is less than six years of age (and we will know, including fractions, how old they are at enrollment by collecting their date of birth); measurement occasion six will occur at least three years after enrollment. Using these conditions, those who enroll on their third birthday will be at least six years old at measurement occasion six (and everyone else will be older); in this scenario it is reasonable to assume that most subjects who enroll at age three will have reached adiposity rebound by measurement occasion six, although we will miss some children who have earlier/later rebound timing. Also, virtually all children who enroll at age four should experience adiposity rebound during the study, but a few might be earlier than four or later than seven. Finally, the majority of those who enroll at age five should experience adiposity rebound during the study, but a minority will have rebounded prior to age five. Note that the mean age at adiposity rebound is a simple function of the coefficients from the main model: $-\beta_2/(2*\beta_3)$ will be the nadir for the control group (and a similar calculation captures the intervention group:

   $-\beta_4/(2*\beta_5)$).

2) The effect of parental change in BMI over the study period on child's growth trajectory: In this study, this effect will be modeled by including baseline BMI of the parent as a predictor, and also including other measures of parent BMI as time-varying covariates (i.e., the value of the covariate depends on the measurement occasion).

3) We will test the difference between mean BMI for both groups at the end of the trial (36 months) to determine whether they are significantly different from one another, thus adding additional information to our analyses.

4) We will test whether the trajectories of both normal and overweight children in the treatment group accelerate at a slower rate than those in the control group over time, such that those in the treatment group will be less likely to evidence trajectories of obesity compared to those in the control group. Each child will be categorized as having, or not having, an acceptable BMI trajectory. This binary variable will be the outcome variable for this secondary analysis. We will test this first, in an unadjusted analysis (a 2 by 2 table where one variable is the outcome variable and the other is group [control or treatment]), and then in an adjusted analysis using logistic regression. Predictors in the logistic regression will include demographics (e.g., gender) and various baseline variables, including the baseline BMI weight category (i.e., normal or overweight).

5) In a series of secondary analyses, we will examine the random-effects in more detail:

1. Using our original fitted model, we will impose an independent covariance matrix (which assumes no correlation between random effects), reducing the resulting number of random effects from seven to five. The results of this change to the model will inform us about the next two steps (see below).
2. We will add the two age-squared terms (for intervention and control) as random effects, continuing to use the independence structure, and bringing the number of random effects back to seven.
3. Keeping the two age-squared terms as random effects, we will return to an unstructured covariance matrix, bringing the number of random-effects to 13.
4. At each step in the above process, we will evaluate the results of continuing to add additional random effects terms, including noting model convergence problems. While we believe the model with 13 random effects will have reduced power and thus do not propose this model for our primary analysis, we believe that fitting this model in a secondary analysis, via the systematic steps outlined above, will allow us to examine the consequences of including a large number of random effects and determine the viability of this alternate model.
5. It is possible that in addition to different ICC's per condition, variability may occur across sessions within condition, such that a range of ICCs exists. If that range is determined to be sufficiently wide, we will consider adding cluster-adjusted standard errors for both the fixed and random-effects. Note that this type of standard error is a generalization of the traditional sandwich estimator; StataCorp has provided a FAQ on this generalization with citations: http://www.stata.com/support/faqs/stat/robust_ref.html.

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Additional Analyses

Secondary Analyses in relation to the Secondary Aims and Hypotheses

In addition to the above analyses, we will conduct analyses necessary to support our secondary aims of the trial, as outlined below.

Aim 2: Compare the effect of the intervention in children who made significant changes in their dietary and/or physical activity behaviors to the effect in children who did not.
Hypothesis 2: Relative to children in the control condition, children participating in the treatment condition will:

2.1 Have lower sedentary activity levels (as measured by actigraphy data) after the intensive phase of the intervention (T2) and at study completion and/or

2.2 Have better adherence to age-specific USDA nutrition recommendations, (e.g., age-appropriate total calories increased, fruits and vegetables, decreased sugar sweetened beverages [measured via diet recall data]), after the intensive phase (T2) and at study completion.

Analysis:

(2.1) A multiple regression model in which child sedentary activity level is regressed on group, controlling for baseline sedentary activity level and including other relevant covariates (e.g., child gender), will be fit at T2 and at study completion.

(2.2) Each child will be categorized as evincing, or not evincing, adherence to age-specific USDA recommendations (as defined in the hypothesis). This binary variable will be the outcome variable for this secondary analysis. We will test this first in an unadjusted analysis (a 2 x 2 table in which one variable is the outcome variable and the other is group [treatment or control]), and then in an adjusted logistic regression analysis predicting adherence category membership and including appropriate covariates (e.g., gender, baseline BMI) in addition to group.

Aim 3: Evaluate the effect of parents' physical activity levels and dietary behaviors on children's levels of the same.

Hypothesis 3: Parents who have significantly lower sedentary activity levels (compared to baseline) after treatment or who have better adherence to USDA nutrition recommendations (age-appropriate total calories increased fruits and vegetables, decreased sugar sweetened beverages [measured via diet recall data]) will be more likely than parents who have higher sedentary activity levels or who do not adhere to USDA nutrition recommendations to have children who will show

3.1: Decreased sedentary activity levels post-treatment and

3.2: Better adherence to USDA nutrition recommendations (as measured in 2.2, above).

Analysis:

Two binary predictors will be created denoting whether parents have significantly lower sedentary activity compared to baseline (yes/no) and whether they have appropriate versus inappropriate dietary adherence (yes/no). These dichotomous variables will be entered into models as follows:

(3.1) A multiple regression model will be fit at T2 and at study completion in which child's sedentary activity level is regressed on group, controlling for baseline child sedentary level, and including the parent dichotomous variables, and two two-way interactions between the parent variables and group (treatment or control) (and including other relevant covariates [e.g., gender]).

(3.2) A logistic regression model will be fit at T2 and at study completion in which the binary child adherence variable (see hypothesis 2.2) is regressed on group and including the parent dichotomous variables and two two-way interactions between the parent variables and group (treatment or control)

(and including other relevant covariates [e.g., gender]).

Aim 4: Explore the potential for developing new social networks and their effect on child nutrition and physical activity.

Hypothesis 4: Parents in the treatment group will develop new social networks and the strength of those social networks will be positively associated with reduced sedentary activity levels and improved dietary behaviors (measured as indicated above) among both parents and children.

Analysis:

A social network analysis will be conducted to determine the strength and cohesion of parents' reported networks. The effect of these networks on parental and child sedentary activity levels and dietary behavior will be estimated. Social network analysis will be conducted using the software packages UCINET and In-Flow. UCINET will be used for entering and analyzing network data and, along with In-flow, for generating network measures and graphical displays. This data set will thus contain both network and attribute variables at the individual level of analysis. Applying standard statistical techniques (e.g., regression, logistic regression, etc.) these independent variables will be modeled with selected dependent variables. The analysis will examine the change in these social networks over time and their impact on the main outcomes of interest including: growth trajectories (children's BMI); body composition (child and adult), parenting practices (child feeding); physical activity (child and adult), and total energy intake. The social network hypothesis suggests that members of a given network group will share health behavior characteristics more than members of other groups.

Aim 5: Evaluate the moderating relationship between genetic risk factors and child BMI trajectories over the course of the study.

Hypothesis 5: Higher levels of child genetic susceptibility to obesity (i.e., a higher genetic risk score (Kathiresan, Voight et al. 2009)) will be significantly associated with heavier-for-age BMI at baseline, and this susceptibility will moderate children's growth in BMI over time.

Analysis:

"Heavier-for-age-BMI at baseline", the outcome, will be regressed on genetic risk score and the interaction between risk score and time, controlling for other covariates as deemed important (e.g., child gender, etc.).

Aim 6: Assess the degree to which implementation of the GROW program encourages additional lifestyle programming for preschool children and their parents in the Metro Community Centers.

Hypothesis 6: The two Metro Community centers participating in the GROW trial will implement a higher number of activity or nutrition programs for families (as defined by the centers) with young children at the end of the study compared to the number they implemented at baseline,

and they will also implement a higher number after the study compared to the number implemented by non-participating Metro Community Centers.

Analysis:

A simple count of the number of activity and nutrition programs will be taken at baseline within both Community Centers (i.e., East and Coleman) and then again at the end of the study to determine whether the number at study end within each center exceeds that at baseline. Similarly, counts will be taken of these types of programs at non-participating Metro Community Centers at baseline and study end and these numbers will be compared to counts at both East and Coleman to determine if both participating centers have higher numbers than the non-participating centers at baseline and at study end.

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Summary of all Amendments of the GROW Trial

IRB amendments were used in the GROW Trial when changes were proposed from the original plan in any part of the research study including study design, informed consent procedures, or any revisions to the approved research protocol. These changes were proposed and only implemented until the Principal Investigator received final written IRB approval. All amendments involved minor changes that pose no more than minimal risk to subjects. Below are the critical IRB amendments requested for the GROW Trial and sorted in chronological order. Others not included are minor requests (e.g., changes in key study personnel, updating Spanish translations of informed consent documents, etc.).

Approval Date	Amendments
6/12/12	Adding an online survey for recreational leaders
7/12/12	1) Changing the names of both treatment groups from the "full" group (intervention arm) to "GROW Healthier" and the "lite" group (control arm) to "GROW Smarter". 2) Using StarPanel as a potential retention tool for families that have been lost at final data collection point (T6).
7/31/12	Adding performance sites not engaged in research as potential recruitment areas.
9/19/12	1. Adding an additional procedure (i.e., Geographical Information Systems (GIS)) to correlate between macro-level built environment data from external sources (i.e., Metro Planning Department) of participants' home address to their perceived built environment (i.e., barriers to physical activity survey data). 2. Revising parental informed consent form to clarify risk for participants.
12/18/12	1. Adding additional performances sites as potential recruitment areas. 2. Changing recruitment strategy from 3-waves to a rolling recruitment cohort strategy. 3. Including the availability of make-up phone call sessions for all intervention family participants in the intensive phase and including the availability of make-up data collection sessions for all intervention and control family participants, at all 6-data collection sessions, which may include participant's homes, if they prefer.
1/18/13	Offering preliminary data collection at convenient locations including the participants' homes, if requested.
2/15/13	1) Using associated visuals during the consent process to increase participant comprehension efficiently with low-literacy targeted participants. 2) Updating pre-screen eligibility scrips 3) Revising raffle incentives implemented during the intensive phase of the intervention.
3/8/13	Adding an additional recruitment strategy whereby participants will receive a small compensation for successfully enrolling participants, based on their referrals.
3/19/13	Implementing text messages by research staff to remind study participants of upcoming sessions and providing them with information relevant to the study aims (i.e., promoting health and/or school success).
5/14/13	Using child's height and weight pre-screening data for baseline data collection.
8/20/13	1. Changing the timing (i.e., data collection points) on our cognitive assessments; and 2. administering quality control measures on a random number of participants and compensating them with a $10 gift card.
4/22/14	Adding 30 additional parent/child dyads for study participation.
5/20/14	Offering an invitational letter to lost study participants that allows opportunities for them to be re-engaged during the maintenance and sustainability phases of the study.
6/5/14	Adding new ancillary study aims: 1) ACTIVATE (a sub-cohort that invites family members to participate in a brief survey at T5 and T6 related to social networks); and 2) GROW Baby (a

	sub-cohort that invites family members that become pregnant to participate in a study that compares pregnancy medical records to study outcomes).
1/21/15	Revising informed consent to further increase clarification of risk when participating in other community-led programs not related to study.
3/24/15	Adding 6 questions to an existing and previously approved survey for our study participants, measuring maternal diet and physical activity during pregnancy.
7/14/15	Adding an additional parental consent form at the last data collection time point (i.e., T6) to obtain a second round of saliva from the existing child participants.
10/1/15	1. Increasing the amount of compensation for our study participants at T5 and T6 (up to $100) to complete certain data elements. 2. Inviting participants to participate in the trial for another follow-up year (T7)
5/18/17	Requesting a Certificate of Confidentiality for all of our study participants

Original Statistical Analysis Plan

Reviewed and approved by the DSMB in April, 2012

$BMI = \beta_0 C + \beta_1 I + \beta_2 (age\text{-}X)C + \beta_3 (age\text{-}X)^2 C + \beta_4 (age\text{-}X)I + \beta_5 (age\text{-}X)^2 I + \ldots + error\ terms$

where:

"I" is an indicator for group and equals 1 for the intervention group and 0 for the control group;

"C" is an indicator for group and equals 1 for the control group and 0 for the intervention group; there is no intercept in this model in the 'traditional sense' (see point 2 below);

"X" is the value at which we center age; we plan to use age at enrollment as our centering term, which will make the indicator variables interpretable (β_0 as the mean BMI at enrollment for those in the control group and β_1 as the mean BMI at enrollment for the intervention group);

"..." stands for other predictors; at the present time, we believe that the predictors for the main model will be gender (coded, e.g., as 1 for female and 0 for male) and ethnicity (we expect there to be 3 ethnicity groups and thus 2 indicator variables for these); in addition, gender by age interaction terms will be included, since the literature indicates that trajectories may differ by gender;

For the primary analysis, "error terms" will include subject, subject X age, and the covariance between these random effects, using a heterogeneous variance structure for the fitted model (Roberts & Roberts, 2005). For the primary analysis, we will not include a random effect for subject X age^2, given that, with our proposed unstructured covariance matrix, the inclusion of this additional random effect would result in 13 random-effects components and may lead to convergence problems (see Rabe-Hesketh & Skrondal, 2012, page 348). We will examine the consequences of this choice via planned secondary analyses.

A post-hoc test of whether $\beta_3 = \beta_5$ will allow us to examine whether the quadratic terms differ between arms of the trial, thus answering our primary research question.

Interpretation of some terms: the indicator variable for trial arm, the linear term (age) for trial arm, and the quadratic term (age)^2 for trial arm jointly describe the trajectory (and starting point) for each group (intervention and control), and each can be interpreted as follows: the constant is the mean BMI at age on entry into the trial; the linear term indicates the rate of change at entry age; and the quadratic term indicates change in rate of growth (acceleration). In our specification, this model allows each child to have her/his own BMI intercept at baseline and own BMI trajectory. Accordingly, we do not include BMI at baseline as a predictor in our model. Additionally, we do not include a BMI by treatment interaction, because BMI is an outcome and treatment is a predictor. We plan to examine a baseline BMI by treatment interaction (as well as other interactions) in our secondary analysis.

Our hypothesis is that β_5, the quadratic term for the intervention group, will be significantly different from β_3, the quadratic term for the control group, at the 0.05 level. We do not have an

hypothesis about the linear terms. Note that we expect the sign of β_5 to be positive, and we expect the coefficient to be smaller than the coefficient for β_3.

Final Statistical Analysis Plan

Finalized in November, 2016

Study Design

The design of the study is a longitudinal non-blinded (open) randomized control trial. Within each of two sites, adult-child dyads with children ages 3-5 years will be randomly assigned, stratified according to parent language use (English or Spanish), to either the three-year prevention program or the control condition. Assessments will occur over 6 time points within each cohort, beginning at baseline and including assessments post-intervention (at 12 weeks/3 months), and at 9, 12, and 36 months from baseline.

Primary Research Question and Hypothesis

Our primary research question is about the impact of the GROW trial on the growth rate of children's BMI over time. Specifically, we hypothesize the following:

Hypothesis 1: The BMI trajectories of children in the treatment group will change at a slower rate than those in the control group over time.

Primary Outcome

Although childhood obesity is a well-documented public health concern, most studies have assessed the obesity outcome (e.g., BMI) using only a single time point or incorporating a pre-post design, leaving us with little knowledge about the actual shape or growth rate of trajectories of BMI during this critical period of development. Indeed, few studies have taken a developmental perspective in order to understand how and when obesity develops in early childhood. By measuring BMI at multiple time points, we will examine growth trajectories in early childhood.

* * *

Because clinical literature about childhood obesity indicates that the shape of the BMI trajectory across ages 3 to 8 is curvilinear, we will account for this in our analytic plan.(Kuczmarski, Ogden et al. 2002; Cole 2004) (see below).

Primary Analysis

Statistical model and approach

Our primary analysis will be an intent-to-treat analysis, and we will fit a multilevel mixed-effects linear model using a maximum likelihood procedure to handle missing data.

Time-varying BMI will be the outcome at Level 1 nested within children at Level 2. Time at Level 1 will be in years since baseline as computed from the date of each child's measurement at each time point. The following child-level (Level 2), time invariant variables will be predictors of the linear and quadratic BMI growth rates and the intercept at Level 1: age at baseline (centered at a value of interest) and random assignment to intervention or control. Child gender will be a child-level (Level 2), time invariant predictor of the intercept at Level 1. This approach allows the estimation of growth rates based on each child's individual measurement dates, and accounts for both age at baseline and time in the study.

The Level 1 equation is as follows:

$$BMI_{ti} = \pi_{0i} + \pi_{1i}(Time)_{ti} + \pi_{2i}(Time)^2{}_{ti} + e_{ti}$$

where BMI for each child *i* is repeated over time *t*. BMI for a given child is a function of the individually varying baseline intercept π_{0i} , the linear growth rate π_{1i} across 36 months, the quadratic growth rate (acceleration) π_{2i} , and a random error term.

The intercept and two growth parameters will then be regressed on Level 2 (child-level) predictors as follows:

BMI Intercept: $\pi_{0i} = \beta_{00} + \beta_{01}(age - C)_i + \beta_{02}(I)_i + \beta_{03}(F)_i + r_{0i}$

Linear Growth: $\pi_{1i} = \beta_{10} + \beta_{11}(age - C)_i + \beta_{12}(I)_i + r_{1i}$

Quadratic Growth: $\pi_{2i} = \beta_{20} + \beta_{21}(age - C)_i + \beta_{22}(I)_i + r_{2i}$

where *I* is an indicator for group assignment and equals 1 for the intervention group and 0 for the control group, and *F* is an indicator for sex and equals 1 for females and 0 for males. β_{00} is the mean initial BMI in control group males while adjusting for child age at baseline (centered), β_{01} is the effect of child age at baseline (centered) on initial BMI, β_{02} is the effect of being assigned to the intervention group on initial BMI (expected to be 0), β_{03} is the effect of being female on initial BMI, and r_{0i} is the random error variance. β_{10} represents the linear growth rate at baseline in the control group while adjusting for child age at baseline, and β_{11} is the effect of child age at baseline on linear growth. β_{12} is the intervention effect on linear growth, and β_{22} is the intervention effect on BMI acceleration while adjusting for child age at baseline.

The Level 1 and Level 2 equations can then be combined and regrouped to yield a single equation for the model:

$$\begin{aligned} BMI_{ti} = {} & [\beta_{00} + \beta_{01}(age - C)_i + \beta_{02}(I)_i + \beta_{03}(F)_i] \\ & + [\beta_{10}(Time)_{ti} + \beta_{11}(age - C)_i(Time)_{ti} + \boldsymbol{\beta_{12}}(I)_i(Time)_{ti}] \\ & + [\beta_{20}(Time)^2_{ti} + \beta_{21}(age - C)_i(Time)^2_{ti} + \boldsymbol{\beta_{22}}(I)_i(Time)^2_{ti}] \\ & + [r_{0i} + r_{1i}(Time)_{ti} + r_{2i}(Time)^2_{ti} + e_{ti}] \end{aligned}$$

where the terms in the first bracket contribute to the intercept, the second bracket's terms contribute to the linear growth, the third bracket's terms contribute to the quadratic growth, and the final bracket contains all of the random error terms. We will specify an unstructured variance-covariance matrix.

We will conduct a likelihood ratio test with two degrees of freedom to test whether the linear and quadratic intervention effects (β_{12} and β_{22}, respectively) are jointly equal to zero. If this joint test is not significant at p<0.05 then intervention effectiveness is not demonstrated. If this joint test is significant at the p<0.05 level, then the intervention effect was significant.

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

With 6 repeated measurements, some participants inevitably will miss one or more occasions of outcome data collection. One advantage of the mixed models over older repeated measure ANOVA models is the use of all available data without dropping any subjects (Nich and Carroll 1997).

References

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Summary of Primary Analysis Adjustments, Clarifications and Specifications

All changes were made with all study personnel still blinded to non-baseline data aggregated by group, including the site-statisticians.

The original analysis plan specified what we thought the predictor variables would be at the time. We have now finalized the included predictor variables for the primary analysis plan. We still adjust for age at baseline and gender, but we do not adjust for ethnicity because of the relative homogeneity of our recruited sample.

Gender is a predictor of the intercept (i.e., initial BMI), and we no longer include a gender by age interaction. This is because the literature shows that girls have a lower BMI intercept than boys at a given age, but the overall shapes of their respective growth curves are comparable.

The revised plan has clarified that the age predictor is baseline age, and time is longitudinal follow-up representing the time a child was exposed to the intervention or control.

The original plan specified that post-hoc secondary analyses would be conducted to determine the potential effect of using different methods for handling missing data (e.g., multiple imputation [MI] with and without auxiliary variables), and we still plan to do this. The current plan makes it clear that we will be using a maximum likelihood (ML) procedure to handle missing data in the primary analysis.

The original primary hypothesis was that the quadratic term for the intervention group will be different from the quadratic term for the control group at the $p<0.05$ level. There was no hypothesis for the linear term. In the current plan we will conduct a likelihood ratio test with two degrees of freedom to test whether the linear and quadratic intervention effects are jointly equal to zero. Intervention effectiveness will be demonstrated if this joint test is significant at the $p<0.05$ level. We made this change because both the linear and quadratic terms determine the overall shape of the outcome curve, and this approach is consistent with typical growth modeling (Singer & Willett, 2003). It is critical to note again that this determination was made with all study personnel blinded to non-baseline data aggregated by group, including the site-statisticians.

The original analysis plan proposed a heterogeneous variance structure, allowing for the ICC at the level of session to be estimated separately for the intervention arm and not for the control arm (because control participants are not assigned to group sessions). We have since decided to model a homogeneous variance structure in the primary analysis; we will explore for a potential heterogeneous variance structure in secondary analyses.