

1 This Clinical Trial Protocol contains the following items:

2

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

4

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

7

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102
103

104 **Original Protocol**

105

106 **Specific Aims**

107 This research includes one primary and five secondary specific aims:

108

109 *Primary Aims:*

110 **1. Aim 1:** Evaluate the efficacy of a multi-level intervention, addressing nutrition and
111 physical activity, at public community recreation centers with high-risk parent- preschool
112 child (ages 3-5) dyads to promote pediatric obesity prevention.

113 **1.1. Hypothesis 1:** The BMI trajectories of children in the treatment group will accelerate
114 at a slower rate than those in the control group over time.
115

116 *Secondary Aims:*

117 **2. Aim 2:** Compare the effect of the intervention in children whose parents made
118 significant changes in their dietary and/or physical activity behaviors to the effect in
119 children whose parents did not.

120 **2.1. Hypothesis 2:** Relative to children in the control condition, children participating in
121 the treatment condition will:

122 **2.1.1.** Have lower sedentary activity levels (as measured by actigraphy data) after
123 the intensive phase of the intervention (T2) and at study completion and

124 **2.1.2.** Have better adherence to age-specific USDA nutrition recommendations,
125 (e.g., age-appropriate total calories increased fruits and vegetables, decreased
126 sugar sweetened beverages [measured via diet recall data]), after the intensive
127 phase (T2) and at study completion.
128

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

131 **3.1. Hypothesis 3:** Parents who have significantly lower sedentary activity levels
132 (compared to baseline) after treatment and who have better adherence to USDA
133 nutrition recommendations (age-appropriate total calories increased fruits and
134 vegetables, decreased sugar sweetened beverages [measured via diet recall data])

135 will be more likely than parents who have higher sedentary activity levels and who
136 do not adhere to USDA nutrition recommendations to have children who will show

137 **3.1.1.** Decreased sedentary activity levels post-treatment and

138 **3.1.2.** Better adherence to USDA nutrition recommendations (as measured in 2.1.2,
139 above)
140

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

143 **4.1. Hypothesis 4:** Parents in the treatment group will develop new social networks and
144 the strength of those social networks will be positively associated with reduced
145 sedentary activity levels and improved dietary behaviors (measured as indicated
146 above) among both parents and children.
147

- 148 **5. Aim 5:** Evaluate the moderating relationship between genetic risk factors and child BMI
149 trajectories over the course of the study.
150 **5.1. Hypothesis 5:** Higher levels of child genetic susceptibility to obesity (i.e., a higher
151 genetic risk score)¹ will be significantly associated with heavier-for-age BMI at
152 baseline, and this susceptibility will moderate children’s growth in BMI over time.
153
- 154 **6. Aim 6:** Assess the degree to which implementation of the GROW program encourages
155 additional lifestyle programming for preschool children and their parents in the Metro
156 Community Centers.
157 **6.1. Hypothesis 6:** The two Metro Community centers participating in the GROW trial
158 will implement a higher number of activity and or nutrition programs for families (as
159 defined by the centers) with young children at the end of the study compared to non-
160 participating Metro Community Centers.
161

162 **Background**

163 ***Early childhood is a critical time for obesity prevention.***

164 Changes in physical activity and diet, among many other factors, have contributed to epidemic
165 levels of childhood obesity in the U.S.²⁻⁶ Obesity rates have tripled among children and
166 adolescents over the past thirty years^{7,8}, with Latino and African-American populations at
167 disproportionately higher risk.^{4,8,9} At the current rates of childhood obesity, 30 to 40% of today’s
168 children may eventually develop type 2 diabetes and reduce their life expectancy.¹⁰ Nader et al
169 demonstrated that children who were ever overweight during the preschool period were five
170 times as likely to be overweight adolescents.¹¹ And the chances of overweight increases as the
171 child ages. In that same study, 80% of school-age children who were ever overweight during
172 this period went on to become overweight adolescents. The significance of mounting risk for
173 sustained overweight and its consequences cannot be overstated. In the Harvard Growth Study,
174 overweight adolescents as adults had a two-fold increase in all-cause mortality and an
175 increased morbidity due to cardiovascular disease.¹² It is not merely overweight/obesity in
176 childhood that poses the risk for later increased mortality and morbidity as an adult, **the slope**
177 **of early weight gain is a potent predictor.**^{13,14} For example, Leunisson et al showed that rapid
178 weight gain without concomitant growth in height during the first three months of infancy is
179 linked with reduced insulin sensitivity in early adulthood. **Furthermore, Barker et al**
180 **demonstrated that the risk of adult coronary events was more strongly related to the**
181 **rapid childhood gain in BMI than to BMI attained at any particular age.**¹³ **Consequently,**
182 **this proposal will address prevention of rapid BMI gain during early childhood, fostering**
183 **normal growth for those children who have a normal BMI (>50% and <85%) and**
184 **improving BMI trajectories for those children who already have a BMI ≥ 85% <95% at**
185 **ages 3-5 years.** There is little evidence documenting successful behavioral interventions to
186 prevent early childhood obesity¹⁵⁻¹⁷ and even less evidence concerning which factors may be
187 crucial to success. Consequently, the Institute of Medicine (IOM)^{18,19} and the *Strategic Plan for*
188 *NIH Obesity Research*^{20,21} call for a community-engaged, culturally-relevant, family-centered
189 approach to obesity prevention that can be sustainable.

190

191 ***Family plays a crucial role in pediatric obesity prevention.***

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

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

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

218 ***Obesity is impacted by both the physical and social environment.***

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

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

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

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

268
269 ***Genetic factors play a role in the development of obesity.***
270 New research demonstrates a genetic risk score (GRS) is a potent predictor of BMI.
271 Family studies have demonstrated that genetic factors account for anywhere between 40% and
272 70% of the population variance in BMI for individuals with severe obesity.^{46,47} Until recently,
273 specific genes contributing to BMI in the general population had not been identified. It is now
274 clear, however, that certain gene variants exert a substantial, clinically important effect on BMI
275 in humans.⁴⁸ The GIANT Consortium recently reported the results from large scale studies to
276 identify genetic variants contributing to the risk of obesity in both children and adults. In January
277 2009, this consortium reported a meta- analysis involving over 100,000 patients, in which 8
278 obesity-related risk alleles were conclusively validated far in excess of the standard (5×10^{-7})
279 for genome-wide statistical significance.⁴⁸ Moreover, whereas each particular obesity
280 susceptibility variant confers only a modest effect on BMI, a genetic risk score summing each
281 individual's number of susceptibility variants across all 8 genes is a more potent predictor of
282 obesity.⁴⁸ Table 1 below provides the details of the validated genetic associations, specifying
283 the effect of each variant (allele) on BMI. All of the genes are on different chromosomes
284 (unlinked), and therefore, were treated as an independent variable. Given that humans have
285 two copies of every autosomal gene, each person has 0, 1, or 2 risk alleles at each locus, with a

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

294
295 Prevention must occur in preschool given that 60% of overweight preschoolers will go on to
296 become overweight adolescents.¹¹ By conducting and testing trials in public community
297 centers, exportable interventions could result allowing for a macro-level system change to
298 address this expanding public health crisis. **Building on the success of an existing
299 partnership between Vanderbilt Pediatrics and Metro Parks and Recreation in Nashville,
300 TN, the team in this proposal will conduct and evaluate an intervention intended to
301 prevent obesity in preschoolers in an approach that affects multiple levels of risk and is
302 both family-based and community-centered. This research includes the following
303 innovations:**

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

315

316 **Recruitment**

317 We will recruit 600 adult parents-preschool child dyads (p/c dyads) to participate in this study for
318 3-years in duration (**see appendix B for recruitment script**). To help manage flow of
319 participants at our community center and library performance sites, our sample (n=600 p/c
320 dyads) will be broken down into 3 cohorts of 200 p/c dyads each. **See Table 1 for breakdown
321 of cohort study implementation design.** Therefore, recruitment efforts will be on-going every
322 year for the first 3-years to actively recruit 200 p/c dyads for each cohort (n=200 p/c dyads per
323 cohort). In order to preserve internal and external validity of the study, the success of any
324 behavioral intervention is contingent on the researcher's ability to recruit and retain study
325 participants. Successful retention of this longitudinal study begins at recruitment.

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

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

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

353 From our GROW formative research pilot (IRB No. 100591), out of 439 parent/child dyads
354 assessed for eligibility, only 50 parent/child dyads were eligible and participated at baseline; a
355 10% return on investment. Due to the challenge of enrolling in a large, longitudinal, community-
356 based, prevention trial, another strategy of recruitment will include outreach to patient families
357 seen by either the Vanderbilt Pediatric Primary Care Clinic or surrounding community practices.
358 To improve efficiency in light of our restrictive eligibility criteria, we will use Vanderbilt’s
359 StarPanel, a computerized electronic medical record database and Vanderbilt’s Whiteboard, a
360 scheduling database, to generate lists with scheduled clinic dates of potential participants that
361 meet BMI, age and zip code eligibility criteria.⁵⁰ Specifically, clinic staff will provide a list of
362 participants to research staff that meet eligibility criteria which serves as a pre-screen to identify
363 targeted, potentially eligible, participants and invite them into the trial. With these lists, we will
364 also send out an invitation letter to prospective participants that includes an opportunity to opt-
365 out recruitment efforts whereby these families that do not wish to be called or approached in
366 clinic’s waiting room, may contact research staff to opt out of receiving any recruitment phone
367 calls or being approached on-site at clinic (**see appendix D for the invitation letter**).

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

376

377 **Informed Consent**

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

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

395

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

404

405 **Inclusion Criteria**

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

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

- 422 • Residence in one of two Nashville regions: **East Nashville/Region 1 (37206, 37207,**
423 **37208, 37213, 37216, 37228)**: surrounding the East Community Center and **South**
424 **Nashville/Region 2 (37013, 37204, 37210, 37211, 37217, 37220)**: surrounding the
425 Coleman Recreation Center

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

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

438 **Exclusion Criteria:**

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

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

451
452 **Child:** Developmentally normal three-to-five year old children with a BMI ≥ 50% and <95%.
453

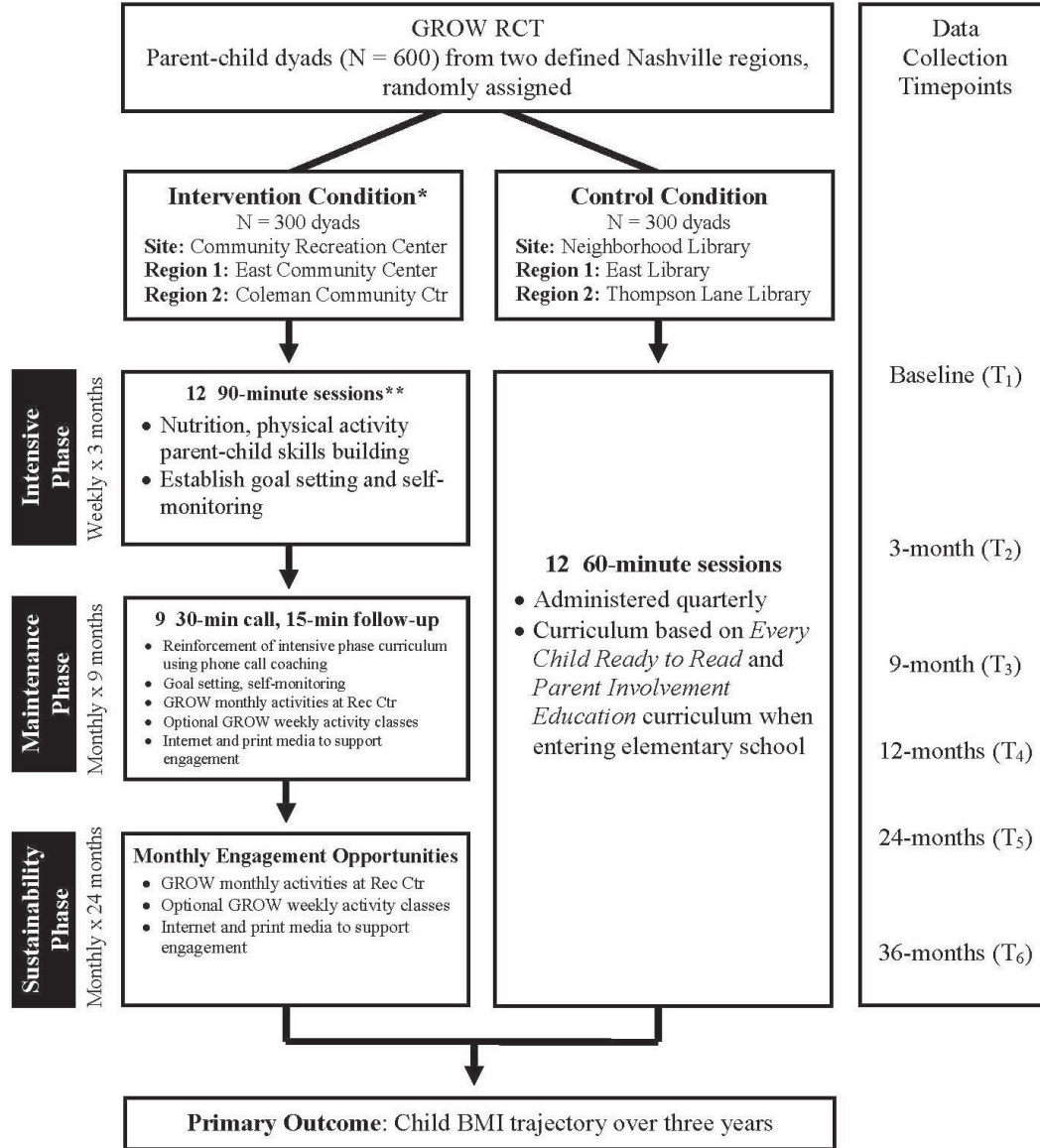
454 **Adult:** Healthy (without medical conditions necessitating limited physical activity) adults age 18
455 or older and designated as the child’s parent or legal guardian.
456

457 **Family:** Speaks English or Spanish, resides in the defined vicinity of the intervention community
458 center or control library, has a commitment to the 3-year study, has phone access, and resides
459 in a household that participates in an assistance program for the underserved (e.g. TennCare,
460 WIC, SNAP, free/reduced price school lunch).
461

462 463 ***Study Procedural Overview***

464 465 **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

466
467

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

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

479
 480
 481

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

482

483 *Study Treatment Groups*

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

503

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

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

515
516 Data collection sessions will be conducted for both treatment groups at 6-points in time (T₁-T₆):
517 baseline, 3-months, 9-months, 12-months, 24-months, and 36-months. Each of the six data
518 collection points in this study will be conducted on-site at either community recreational center
519 (i.e., Coleman and East Park) with Metro Parks staff and research staff. Metro Parks staff will
520 not be “engaged” with research but will handle flow, childcare and check-in with participants.
521 This data collection process will involve adult-child dyads to proceed through a variety of
522 stations to gather measurements and information for study analysis.

523
524 *Facebook use throughout the study for the Intervention Group*
525 Since our targeted population are underserved families, such families have been well-known in
526 the literature to be hard-to-reach and hard-to-keep families, especially over a 3 year period of
527 time. Because of this challenge, Facebook has been considered a viable tool to retain and
528 reach families, in addition, serve as an interactive tool to continually maintain engagement for
529 participants in the GROW study (**see appendix H for Facebook messages**). Thus, all study
530 participants in the intervention groups will be invited to join a private GROW Facebook group.
531 Specifically, through our group page, members will receive reminders to upcoming
532 sessions/community events, polls to gauge satisfaction and curriculum understanding, posts
533 that display recipes, pictures, and videos, and links to helpful web pages for more information.
534 In addition, Facebook group members will be able to post comments and pictures, and hopefully
535 strengthen their social network ties amongst themselves. This Facebook group page will not be
536 accessible to the general Facebook community nor the community in the control condition. Per
537 Vanderbilt Social Media Policies, research staff will monitor content daily to ensure appropriate
538 discourse and interaction that uphold the standards of Vanderbilt as an institution. For those
539 families that do not have a Facebook account, emails and/or regular mail will be sent out
540 monthly.

541
542 *The Adaptive Intervention Design*

543 The research team plans to utilize an adaptive intervention approach⁵³ for children who are not
544 responding to the intervention based on their BMI trajectories. More simply, for the purposes of
545 this adaptive intervention, a child will be considered a non-responder if her/his BMI weight
546 categorization shifts negatively from T1 to T2 (i.e., if formerly normal weight child shifts to
547 overweight or obese in this period of time; or if formerly overweight child shifts to obese, as
548 defined by BMI). Child BMI change from T1 to T2 will be reported using an easily
549 understandable and comprehensive growth feedback report and mailed to the parents after T2
550 measurements are collected. The adaptive intervention will occur at the first phone call coaching
551 session of the maintenance phase. The coach will review the feedback report with the parent
552 and solicit from the parent both the successes and barriers faced with incorporating GROW
553 lessons into their everyday lives (responders will also receive feedback reports but will not
554 receive a report explanation session discussed by a phone call coach). These adaptive
555 intervention report feedback sessions will occur again after BMI categorization/non-responder
556 status is reassessed at the T3, T4, and T5 data collection time points.

557

558 **Outcome Measures & Procedures**

559 *Primary Outcome*

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

567 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

568

569 *Secondary Outcome*

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

574

575 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			
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576

577 *Collection of Moderators & Mediators*

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

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

590 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
	GROW developed survey questions related to intervention messages	Self-reported physical activity habits	P	Computerized Survey (2Q)	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

	GROW developed survey questions related to intervention messages	Parent and child eating and feeding habits	P	Computerized Survey (8Q)	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	How often meals are eaten together	P	Computerized Survey (3Q)	T ₁ – T ₆
	GROW developed survey questions related to intervention messages	Where meals are eaten together	P	Computerized Survey (3Q)	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	Media available in household	P	Computerized Survey (3Q)	T ₁ – T ₆
	Youth Risk Behavior Survey (YRBS) subscale	Child's media use	P	Computerized Survey (3Q)	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, 4 th 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

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

593 **Process Measures**

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

603

604 **Description of Measures**

605

606 **Anthropometric Measurements**

607 Body weight for each subject will be measured, after voiding and wearing light clothing, to the
608 nearest 100 g on a calibrated digital scale. Body height without shoes will be measured to the
609 nearest 0.1 cm with a stadiometer. BMI will be calculated (weight [kg]/height [m²]), using the
610 standard CDC calculator. Both height and weight measures will be collected twice. The mean of
611 the two closest measures is used as a final measurement. Children will be wearing light clothes
612 and without shoes. Height without shoes will be measured to the nearest 0.1 cm using our
613 standard stadiometer (Perspective Enterprises, Portage, MI). Adult and child waist
614 circumference will be measured with a fiberglass measuring tape on the skin, at the umbilicus,
615 to the nearest 0.1 cm, according to the recommendations of the World Heart Federation.⁵⁴ Waist
616 circumference will be collected two times, if the two measurements of waist differ by 1 cm or
617 more, then the waist measurements are repeated a third time and data entered. The mean of
618 the two closest measures is used as a final measurement. Measurements will be obtained by
619 trained project staff and standardized according to accepted standards.⁵⁵⁻⁵⁷

620

621 **Triceps Skinfolts**

622 Triceps skinfold thickness is a measure of subcutaneous fat and is a component of equations
623 used to predict body fat composition.⁵⁸ SFs have been used successfully in studies with adults
624 and children,⁵⁹⁻⁶¹ including young children from 3 to 8 years of age.^{62,63} Recent literature
625 suggests that SFs are more accurate in estimating body composition compared to bioelectrical
626 impedance (BIA) during the adiposity rebound, the normal pattern of growth that occurs in all
627 children growing between 3 to 5 years of age.⁶² SF is measured using a Lange skinfold caliper

628 in the midline of the posterior aspect (back) of the arm, over the triceps muscle, at a point
629 midway between the lateral project of the acromion process of the scapula (shoulder blade) and
630 the inferior margin (bottom) of the olecranon process of the ulna (elbow). They are measured to
631 the nearest 0.1 mm and collected two times. A third SF measurement is taken if either of the
632 following occur: 1) If the two triceps values are less than 10mm but differ by 2 mm or more; or 2)
633 If the skinfold is 10mm or larger, with a difference between the two measurements of greater
634 than 10% (((maximum-minimum)/minimum)*100). In either case, the mean of the two closest
635 measures is used as the final measurement. In order to accommodate participants that are
636 morbidly obese participants then we will use the Harpenden calipers. Training, certification and
637 quality control procedures for SFs are similar to those outlined above for waist circumference
638 and other anthropometrics.
639

640 Accelerometers

641 Amount of physical activity will be assessed using the ActiGraph GT3M (Actigraph LLC, Ford
642 Walton, FL) accelerometer. Accelerometry had been used successfully in studies with adults
643 and children⁶⁴⁻⁶⁸ with a reliability: $r = 0.93$ ⁶⁹. Both a parent and a child will be asked to wear
644 the monitor for one week during waking and sleeping hours except when bathing, showering, or
645 swimming. A simple 1-page manual (in Spanish and English) will be provided. The monitor will
646 be attached to a belt secured at the waist. The monitors will be sent by mail in pre-addressed
647 and pre-stamped boxes to the Energy Balance Laboratory at Vanderbilt. We have used this
648 technique very successfully in similar studies with children and their families. The activity data
649 will be downloaded to a computer and analyzed. Physical activity will be expressed as activity
650 counts per day. Total and physical activity energy expenditure (kcal/day) will be calculated using
651 validated equations.^{69,70} Threshold values from a validation study will be used to calculate time
652 spent in sedentary, light, moderate, and vigorous activity. Accelerometer use will be
653 supplemented with a short physical activity log that collects physical activities and time of
654 accelerometer use (hours/day).
655

656 Energy Intake

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

674 (eg, >4000kcal/d). Dietary data will be entered and analyzed using our NDS-R software
675 (Nutrient Data System for Research, St. Paul, MN). Added sugars will be calculated using the
676 USDA database (<http://www.ars.usda.gov/Services/docs.htm?docid=12107>)
677

678 Study Questionnaire

679 The study questionnaire will measure a variety of domains and will be provided in both English
680 and Spanish (**see appendix K for survey**). It will be a computer-administered questionnaire
681 completed by parents with paper and pencil questionnaire as back-up. **See Table 4: Collection**
682 **of Moderators & Mediators above for details**. Survey takes about 30-45 minutes to complete.
683

684 Social Networks

685 We will collect social network data, exploring the potential development of new social ties that
686 could result due to the structure of the study (**see appendix L**).
687

688 Genetics

689 Saliva will be collected from the parent-child dyad participating in the study⁷¹. For adults, saliva
690 will be obtained utilizing the Oragene saliva kit, collecting 2-3 cc of saliva per participant. For
691 young children, saliva will be obtained utilizing the “baby brush” approach, in which small
692 sponges attached to plastic handles are inserted between cheek and gumline to absorb saliva.
693 Subsequently, the sponges (x4) are cut and placed in the spittoon with DNA preservation
694 solution. We will then use a modification of the Puregene DNA (Gentra, Inc) Purification
695 Protocol for 4 ml Saliva Samples⁷¹, consisting of 4 stages: (1) cell lysis and addition of RNase
696 to remove RNA from the salivary nucleic acid; (2) DNA precipitation in 100% isopropanol, with
697 70% ethanol wash; (3) DNA hydration in reduced TE (Tris EDTA) to approximate concentration
698 of 200 ng/u; (4) DNA storage at 4C for working stock, and -80C for archival DNA samples.
699

700 Barriers to Physical Activity Questionnaire

701 This study survey is based from the *Environmental Supports for Physical Activity*
702 *Questionnaire*⁷² to assess individual perceptions of physical activity supports in the social and
703 physical environment, use of the built environment, current physical activity behavior and
704 recreation center use. This survey will take about 15-20 minutes to complete and has been
705 validated in previous literature.⁷³ These data will help describe the policy environment of study
706 participants and identify policies that enable or constrain active living for participants. The
707 objective of this survey is to link current behavior with local community policies. Specifically, to
708 determine specific neighborhood characteristics that enable or constrain participant ability to be
709 physically active, match participant responses to one of the three policy types: personal safety,
710 transportation, and land use, describe local and state policies that address participant
711 responses, and identify untapped policy options for improving physical activity levels in
712 participant communities.
713

714 Control Measures

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

719 intelligence of the child participants, the research team will use the Woodcock-Johnson III Tests
 720 of Cognitive Abilities – Brief Battery. This tool involves a battery of tasks where children
 721 expressively (verbally and/or through pointing) respond to an assortment of pictures and words
 722 in a flipbook. Trained data collectors will administer this test individually with each child. The
 723 brief battery is estimated to take between 15 and 20 minutes to administer.
 724

725

726 **Incentives**

727

728 **Data Collection Incentives**

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

734 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

735 *Participants will receive half of the incentive upfront prior to wearing accelerometers and the other half
 736 upon return and completion of at least 2 of the 3 diet recalls.
 737

738 **Intervention Incentives**

739 **Intensive Phase:** Participants will receive tangible tools or small giveaways during each session.
 740 The value of these items will be approximately \$3.50 per parent and child dyad each week when
 741 sessions occur. Examples of tangible tools, items to reinforce lessons learned are kitchen ware
 742 utensils, measuring spoons, etc. In addition to the tangible tools, in order to encourage
 743 attendance during the intensive phase of the intervention (weekly for 3-months), participants will
 744 have an opportunity to enter a raffle. These raffles will be held during sessions 3, 6, 9, and 12
 745 (see table 6 below for details). The odds of winning the raffle in the intervention group is about
 746 1:15, assuming that on average there are 15 people in attendance each week. Notably, the
 747 odds vary based on the number of sessions each person attends individually and the number of
 748 attendees in the session. Moreover, there will be a separate raffle for each intervention group
 749 for each cohort. Specifically, there will be between 6-8 intervention groups per cohort (3-4
 750 groups per site). If participants attend all 12-sessions during the 3-month intensive phase,
 751 participants will receive a value amounted of \$42 worth of small gifts.
 752

753 Table 6: Data Collection Intervention Incentives

754

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

755 *We may substitute items of similar value

756 Note: These items were based on a kitchen inventory administered by our nutrition team. 42-57% of
757 those surveyed did not have these items.

758

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

765

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

777

778

779 Control Incentives

780 Similar to the intensive phase of the intervention incentives, all participants will receive tangible
781 tools or a small giveaway during each session. The value of these items will be approximately
782 \$5.0 per parent and child dyad when sessions occur. Examples of these giveaways are books,
783 etc. If participants attended all sessions for 36-months, participants will receive a value of \$60
784 worth of small gifts. In addition, at every session, all attendees will be entered in a raffle to win a
785 \$20.00 gift card (quarterly for 36-months). Similar to the intervention group, the odds of winning
786 the raffle in the control group is about 1:15, assuming that on average there are 15 people in
787 attendance.

788

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

793

794 Health-related Incentives

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

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

803
804 The value of the parent and child gym membership for one year equates to \$400 at each
805 community center. Although this may be interpreted as undue inducement for families to
806 participate in a 3-year RCT study, providing gym membership to participants allows increased
807 physical activity and healthy living - a direct benefit and positive health advantage to subject
808 participants and their families as opposed to compensation of monetary or economic gains.
809 Since increasing physical activity is directly related to the outcome of the study, we
810 conceptualize offering gym memberships as a bonus and a justified benefit for those that have
811 participated.

812

813 ***Randomization***

814

815 Randomization Schedule

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

822

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

828

829 Random Assignment

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

847

848 Randomization Data Management

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

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

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

866

867 Randomization Data Safety

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

874

875 ***Risk/Benefit Analysis***

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

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

893 center, depending on which treatment group will be during or after study implementation, which
894 allow adults to use the weight room for no cost, and families to take swimming lessons at 50%
895 of the normal cost.
896

897 **Data and Safety Monitoring Plan**

898 899 General Description

900 Comprehensive measures will be implemented to maintain subject confidentiality as
901 appropriate. Study ID number will identify all data collection materials for the study. Only study
902 team members will have access to master linkup lists that match participant names to these
903 Study ID numbers. The master link-up list linking names and Study ID numbers will also contain
904 some basic demographics to be collected for purposes of the study (e.g., gender, maternal
905 education) and personal health information (weight, height, body composition). All data
906 collection forms will be housed at VUMC.
907

908 All study data will be kept at VUMC securely locked in a storage area for this study. All data will
909 be obtained specifically for research purposes. The study investigators reviewing the data will
910 not be provided with any participant identification information. Study data collection forms will be
911 maintained under lock and key for 10 years following completion of the study. Thereafter, they
912 will be destroyed. All electronic data files will be stored on a password protected, secure,
913 encrypted server. Only key study personnel will have access to the password. Ten years after
914 study completion, electronic copies of all datasets will be destroyed. Individuals will not be
915 identified in any publications of the study findings.
916

917 Data Safety and Monitoring Plan

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

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

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

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

933
934 **Probable** (to qualify, the adverse event must meet 3 of the following conditions):

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

- 940
941 **Definite** (to qualify, the adverse event must meet at least 4 of the following conditions):
942 1) has a reasonable temporal relationship to the intervention,
943 2) could not readily have been produced by the subject's clinical state,
944 3) could not readily have been due to environmental or other interventions,
945 4) follows a known pattern of response to intervention,
946 5) disappears or decreases with reduction in cessation of intervention.
947

948 **Policy for Blinding in COPTR**
949 **January 26, 2012**

950
951 **Introduction**

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

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

964 Clarification of terms:

- 965
- 966 • The "study starts" at a site when the first participant is randomized.
 - 967 • The "study ends" at a site when the outcomes (primary and secondary) of importance to
968 the site have been collected on all participants.
 - 969 • "Interim" information is information that is collected between the study start and the study
970 end at a given site.

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

- 972
- 973 • **Common elements** refer to those measures that two or more sites collect, protocols
974 and manual of procedures related to those measures, and reporting processes.
 - 975 • **Site-specific elements** refer to those measures and operational activities that relate to
976 only one site.

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

- 978
- 979 • Study data – any information collected on study participants, which includes
 - 980 ○ Primary and secondary outcome variables
 - 981 ○ Demographic variables
 - 982 ○ Mediators and moderators
 - 983 • Outcome variables – primary and secondary outcomes as described in site protocols
 - 984 • Process variables – e.g. training, recruitment, intervention implementation, fidelity,
985 adherence, retention/attrition

986 Also, data are available at multiple levels:

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

990

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

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

999 There may be specific process data collected in one or more arms that the Principal Investigator
1000 and study staff want to review aggregated by arm before the end of the study. Those variables
1001 will be declared *a priori* by each site, reviewed by the Design and Analysis Working Group, and
1002 approved by the PI. Those variables will be clearly listed as unblinded variables in the final
1003 study protocol. Should sites wish to examine additional blinded process variables aggregated
1004 by arm, after the study has begun, those requests would also be reviewed by the Design and
1005 Analysis Working group and, if access is approved by the PI and by the DSMB, those variables
1006 will be clearly listed as unblinded variables in an amendment to the study protocol. Subsequent
1007 references in this document to process data will distinguish between blinded and unblinded
1008 process variables.

1009 In clinical trials that require **interim** monitoring, it is an accepted principle that interim OMM and
1010 blinded process data aggregated by arm should be kept confidential, with such data accessible
1011 only to a small number of individuals responsible for its analysis and monitoring. Generally,
1012 blinding to intervention arms should be maintained to the extent possible until the study ends.
1013 In COPTR, study investigators and sponsors are not privy to interim OMM and blinded process
1014 data aggregated by arm, and only the study or independent statisticians/analysts preparing and
1015 presenting the analysis to the DSMB, as well as the DSMB, are unblinded.

1016 The study arms in the 4 trials are, BY DESIGN, not able to be totally blinded. However, some
1017 blinding can be maintained. Measurement staff should not be informed of the intervention that
1018 individual participants are receiving, and should have **no role** in the delivery of the intervention.
1019 Efforts should be made to avoid participant (child/parents) interactions that result in open
1020 chatting with assessors about the interventions they have received. Measurement staff should
1021 be trained to end any such communication when initiated by participants.

1022 Study investigators and staff are kept blinded as to the ARM level results until study end. That
1023 is, they should **never** see or hear OMM and blinded process data aggregated by arms until the
1024 DSMB allows it. Exceptions to this policy are made only for individuals and circumstances in
1025 which unblinding is necessary for the preparation of reports to the DSMB. Ancillary studies
1026 need to adhere to these same principles.

1027 **Table 7. Summary of issues related to maintaining objectivity as applied**
1028 **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 <i>a priori</i> or by amendment to the protocol as unblinded	YES

1029

1030 **Guiding principle #3:** In COPTR, the RCU will function as the ‘Independent Statistician,’ while
1031 the individual study center statisticians/analysts will function as the ‘Site Statistician.’

1032 The rationale for keeping investigators and sponsors blinded to interim data is generally
1033 accepted. The possible conflict of interest that could arise for the site statistician or analyst who
1034 performs the analysis of the interim data and presents it to a data monitoring committee has
1035 received little attention. Ellenberg and George (2004) describe some potential conflicts for the
1036 Site Statistician, and approaches that might be taken to minimize them.

1037 Ellenberg & George (2004) argue that a reason for not blinding the Site Statistician is the
1038 assumption that the Site Statistician is someone “with no obvious intellectual conflicts of interest
1039 who, by training and temperament, can be trusted to provide a dispassionate analysis of the
1040 accumulating data.” This objectivity assumption may or may not be true, and there are many
1041 pressures exerted on the Site Statistician that is employed and part of the team at a study site.

1042

1043 Each of the 4 COPTR sites has identified an individual(s) who will serve as the Site Statistician.
1044 The **Site Statistician is the person(s) responsible and accountable** for maintaining the blind
1045 of any site-specific study OMM and blinded process data from all other site study investigators
1046 and staff. It is the responsibility of the site Principal Investigator to ensure that the Site

1047 Statistician understands his/her role and responsibilities. The Site Statistician must have no
1048 communication with others at the site, formally or informally, about trends in OMM and blinded
1049 process data and side effects. They must also safeguard data files, printed output, log files and
1050 any emails or correspondence related to the OMM and blinded process data and side effects
1051 with the RCU and the DSMB. It is their responsibility to take care in destroying printouts and
1052 correspondence – ideally by shredding. It is also their responsibility to make sure that any
1053 discussion and communications of blinded data with the RCU and DSMB are confidential.

1054 The Site Statistician:

- 1055 i. will be blinded to aggregate comparisons by arm of post-randomization COMMON
1056 OMM data until all endpoint data have been collected at their site unless otherwise
1057 instructed by the DSMB.
- 1058 ii. will remain objective when carrying out the activities of conducting the trials –
1059 preparing randomization schemes, randomizing individual subjects, processing of the
1060 data, cleaning and editing the data, preparation of analyses/reports of site-specific
1061 OMM and blinded process data, and transmitting the COMMON OMM data to the
1062 RCU; and
- 1063 iii. is responsible and accountable for maintaining the blind of study site investigators
1064 and staff at their site with respect to OMM and blinded process data aggregated by
1065 arm.
1066

1067 The RCU:

- 1068 i. is the only entity that has personnel that are unblinded to the COMMON OMM data
1069 aggregated by arm during the trial;
- 1070 ii. will prepare analyses/reports to the DSMB of the COMMON OMM data and adverse
1071 events aggregated by arm, as requested by the DSMB;
- 1072 iii. shares responsibility for maintaining the blind of study site investigators and staff;
1073 and
- 1074 iv. is responsible and accountable for maintaining the blind of co-investigators from NIH
1075 and RCU staff who do not need to be unblinded with respect to COMMON OMM
1076 data aggregated by arm in order to complete their duties.
1077

1078 **Responsibilities of the Site Statistician and the RCU**

1079 It is imperative that professional ethical conduct guidelines be followed by the Site Statistician
1080 and the RCU Independent Statisticians at each stage of the study. The Site Statistician
1081 prepares the randomization scheme and thus handles the list (datafile, database table, etc.)
1082 linking study ID to assignment that permits looking at the data aggregated by arm. Thus, this
1083 person(s) must exercise care in protecting the treatment allocation list and ensuring no one –
1084 including him/herself - conducts any analyses of COMMON OMM variables, adverse event or
1085 other follow-up information aggregated by arm. The Site Statistician may prepare descriptive
1086 reports of site-specific data aggregated by study arm if so directed by the DSMB or RCU. All
1087 study data must be protected in secure, password protected files or databases with only the Site
1088 Statistician, their programming staff, and the RCU having access to the data files. Note that
1089 data needed to interact with and track families (e.g., names, ages, contact info, etc), will not be
1090 blinded to interventionists, of course.

1091 The list (datafile, database table, etc.) created by the Site Statistician that contains the subject
1092 ID and the allocation to study arm is protected in a secure and password protected manner with
1093 only the Site Statistician and the RCU having access to the information.

1094 **Blinding of Investigators by Data Type**

1095 All data collected will be categorized *a priori* into one of 7 categories:

- 1096 i. *Demographic* information, such as age, sex, country of origin, and contact
1097 information is not blinded, either at the individual level or aggregated by arm.
- 1098 ii. *Study arm assignment* is concealed until the time of randomization.
- 1099 iii. Post-randomization, all field center or site personnel are blinded to *common OMM*
1100 *data, aggregated by arm*, except as allowed by the DSMB.
- 1101 iv. Post-randomization, all site personnel except the site statisticians/analyst are blinded
1102 to site-specific OMM data, aggregated by arm. The site-specific OMM data,
1103 aggregated by arm, are held strictly confidential by the Site Statistician, programmers
1104 they designate, and the RCU as detailed in this document.
- 1105 v. *Post-randomization, individual level process data* are viewed by the Principal
1106 Investigators throughout the study and may also be shared with the interventionists,
1107 Project Coordinator or Manager. *Arm-level process data* may be viewed by the
1108 Principal Investigators and shared with the interventionists, Project Coordinator or
1109 Manager, if those variables are first reviewed by the Design and Analysis Working
1110 Group, approved for access by the PI, and listed *a priori* as unblinded variables in
1111 the study protocol or as an amendment to the study protocol.
- 1112 vi. Post-randomization, blinded process data, aggregated by arm, are held strictly
1113 confidential by the Site Statistician, programmers they designate, and the RCU as
1114 detailed in this document.
- 1115 vii. *Safety data* are collected for the purpose of insuring participant safety. Guidelines
1116 for viewing these data have been designed by the COPTR Subcommittee on
1117 Recruitment, Retention, Consent, Adverse Events and Safety.
- 1118

1119 **Blinding of Investigators to Study Data by Study Stage**

- 1120 i. **All baseline data** from an individual subject are collected prior to allocation to a study
1121 arm. Following all baseline data collection on an individual subject, allocation
1122 information on that subject is made available to site study staff as needed.
1123 Comparative baseline (pre-randomization) data may be viewed by investigators and
1124 study staff in aggregate by arm (e.g., for reporting comparability of groups in a
1125 design and/or baseline manuscripts). The site investigators may analyze and publish
1126 data collected at baseline using the usual policies of subject confidentiality and
1127 protection and guidelines set by the COPTR Subcommittee on Publications,
1128 Presentations and Ancillary Studies.
- 1129 ii. **Interim Data (post-randomization)**. All site personnel are blinded to *common OMM*
1130 *data, aggregated by arm*, except as allowed by the DSMB. All site personnel except
1131 the site statisticians/analyst are blinded to site-specific OMM data, aggregated by
1132 arm. The site-specific OMM data, aggregated by arm, are held strictly confidential by
1133 the Site Statistician, programmers they designate, and the RCU as detailed in this
1134 document. *Individual level process data* are viewed by the Principal Investigators
1135 throughout the study and may also be shared with the interventionists, Project
1136 Coordinator or Manager. *Arm-level process data* may be viewed by the Principal
1137 Investigators and shared with the interventionists, Project Coordinator or Manager, if

1138 those variables are first reviewed by the Design and Analysis Working Group,
1139 approved for access by the PI, and listed *a priori* as unblinded variables in the study
1140 protocol or as an amendment to the study protocol. Blinded process data,
1141 aggregated by arm, are held strictly confidential by the Site Statistician, programmers
1142 they designate, and the RCU as detailed in this document. **No interim OMM or
1143 blinded process data from any arm are available for publication or
1144 presentation until the end of the study, unless the plan has been (1) reviewed
1145 by the Design and Analysis Working Group and the Publications
1146 Subcommittee and (2) approved by the site PI, the Steering Committee, and the
1147 DSMB.**

1148 iii. *Final data.* *Final data* are held private at each site or at the RCU in the same
1149 manner as the Interim data until the end of the study. The end of the study at each
1150 site is defined as the moment that the last study data point at that site has been
1151 collected and recorded. This includes data from all study index children as well as
1152 data from other individuals and entities at a study site. At the end of the study, all
1153 study data, including data on study arm assignment, can be accessed by study
1154 investigators using the usual policies of subject confidentiality and protection and
1155 guidelines set by the COPTR Subcommittee on Publications, Presentations and
1156 Ancillary Studies.
1157

1158 **Preparation of Study Data Reports for the DSMB**

- 1159 i. Accumulated data will be ‘frozen’ at a specified date for the particular report. A copy
1160 of the ‘frozen raw datafile of COMMON measures’ is sent to the RCU for analysis
1161 along with the protected list of the treatment allocation.
- 1162 ii. After processing, cleaning, editing, creating derived variables, the dated ‘analysis
1163 files’ of COMMON variables (including treatment allocation) and relevant
1164 documentation are sent to the RCU. Site-specific data are not sent to the RCU.
- 1165 iii. For COMMON variables, the Site Statistician conducts analyses for the purposes of
1166 data cleaning and looking for outliers, unusual trends and distributional anomalies of
1167 the data from their own site, overall – **not** by study arm. They do not generate
1168 comparative analyses by study arm. Information generated (not the raw data) may
1169 be shared with other site investigator/s for the purposes of conducting data cleaning.
1170 The cleaned COMMON variables data are sent to the RCU, along with means and
1171 frequencies for all variables. The RCU will prepare means and frequencies for all
1172 variables and compare them to the site results to confirm accurate transfer of data.
1173 The RCU will prepare descriptive and quality control tables for presentation to the
1174 DSMB, both overall and by study arm. No modeling is done by the RCU unless they
1175 are specifically instructed to do so by the DSMB.
- 1176 iv. For **site-specific** data, the Site Statistician conducts analyses for the purposes of
1177 data cleaning and looking for outliers, unusual trends and distributional anomalies
1178 from their own site, in a manner similar to that described above for COMMON
1179 variables. Different from common variables, the Site Statistician prepares descriptive
1180 and qualitative data reports using templates developed in cooperation with the RCU.
1181 These reports will not be generated by study arm unless instructed to do so by the
1182 DSMB. Otherwise, site-specific variables will be examined only with data from all
1183 study arms combined.
1184

1185 **Data on Participant Safety**

1186 As with other data, safety data will be blinded, as possible, to the investigators and staff at each
 1187 site (not possible when obviously related to the intervention or collected during an intervention
 1188 activity, for example). The objectively collected adverse events data, however, are collected the
 1189 same way in all arms and will be blinded. Sites should see only aggregate data (all treatment
 1190 arms combined) although RCU can prepare data for DSMB by arms.

1191 **Treatment condition unblinding recommendations**

1192 Study arms

1193 Decisions to unblind the site investigators to arm-level experimental assignment will be the
 1194 responsibility of the DSMB according to the following steps.

- 1195 i. RCU prepares adverse events and safety reports by unidentified arm (e.g., group A,
 1196 group B) in the twice-yearly DSMB reports.
- 1197 ii. DSMB reviews adverse events and other safety-relevant data at their periodic
 1198 meetings.
- 1199 iii. If the DSMB identifies a potentially important difference between arms in adverse
 1200 events or other safety-related data, they may request additional analyses and/or
 1201 request unblinding of arm assignment (e.g, treatment and control), and may consult
 1202 with the NIH, RCU and PI(s) to help them interpret the findings. Unblinding, if
 1203 necessary, should be limited to only those investigators who need to know to protect
 1204 the safety of participants.
- 1205 iv. If the DSMB determines that the differential between arms may impact the safety of
 1206 participants and/or changes the assessment of risk of participation, they will make
 1207 the appropriate recommendation to the NIH who, in turn, will notify the site PIs,
 1208 accordingly.
- 1209 v. It is the responsibility of the site PIs to report to their site IRBs.

1211 **Presentation of Reports to the DSMB**

1212 The RCU statisticians will be presenting the report, which includes the report on the common
 1213 measures, plus each site’s site-specific variables report. The Site Statisticians are available to
 1214 be contacted by phone during the DSMB meeting in case questions arise that they are in a
 1215 better position to answer about the site-specific variables and the overall site analyses. Site
 1216 Statisticians may not participate in any portion of the meeting or call in which unblinded common
 1217 OMM data are discussed.

1218 **Timeline for preparation of reports to the DSMB**

1219 Typically there is a roughly a 7-week period prior to the date of the meeting for preparing the
 1220 DSMB report. Adherence to this timeline assumes that data entry and cleaning have been
 1221 ongoing and that templates used to generate tables have already been created. It also
 1222 recognizes that some data, such as blood analyses, actigraph, and diet data, that undergo other
 1223 processing, may be delayed in comparison to other types of data.

1224 **Table 8. Timeline for preparation of reports to the DSMB**

-7 weeks	<ul style="list-style-type: none"> • data ‘frozen’ for the report on same date at each field site • copy of raw frozen COMMON measures files sent to RCU
-5 weeks	<ul style="list-style-type: none"> • data processing, data cleaning, data editing, datafile creation at each field site completed • clean COMMON measures files sent to RCU

-3 weeks	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • RCU compiles reports, assembles binders and sends to DSMB
0 weeks	<ul style="list-style-type: none"> • DSMB meeting

1225

1226 At the meeting, the RCU presents the report, and afterwards collects all reports for archival. The
 1227 RCU communicates with site investigators and Site Statisticians on relevant issues raised by
 1228 the DSMB – such communication is not shared with other site staff or investigators.

1229 **Communication of the Policy for Blinding in COPTR**

1230 In order to insure that this policy is clearly understood and communicated, all COPTR study
 1231 Principal Investigators, the NIH Project officer, the Site Statistician and the RCU members
 1232 involved in data management or analysis will confirm compliance. Over the course of the study
 1233 as new personnel are hired, they will also confirm compliance. This will be done by each of
 1234 these individuals sending an email to the COPTR Communications Manager as follows:

1235 I have read, understood and agree to comply with the 9 page document entitled,
 1236 *Policy for Blinding in COPTR.*

1237 The RCU will maintain a list of the names of individuals from whom this confirmation has been
 1238 received, and this list will be available for inspection by the DSMB.

1239

1240 **References**

- 1241 1. Ellenberg SS, George SL (2004) Should statisticians reporting to data monitoring
 1242 committees be independent of the trial sponsor and leadership? *Statistics in Medicine*
 1243 23:1503–1505.
 1244 2. Friedman LM, Furberg CD, DeMets DL (2010) Fundamentals of Clinical Trials, 4th ed.,
 1245 Springer, NY.
 1246

1247

1248

1249 ***Study Design, Statistical Consideration and Analysis Plan***

1250

1251 **Study Design**

1252 The design of the study is a longitudinal non-blinded (open) randomized control trial, comparing
 1253 participants in an obesity prevention treatment program to those in a non-specific literacy-based
 1254 educational control group. The trial will take place over six years. The trial will be conducted at
 1255 two separate sites (region One, East Nashville, and region Two, South Nashville). Within each
 1256 site, parent-child dyads with children ages 3-5 years will be randomly assigned, stratified
 1257 according to parent language use (English or Spanish), to either the three-year prevention
 1258 program or the control condition, yielding 600 dyads per cohort (300 per region/site), and a total

1259 sample size of 600. Assessments will occur over six time points within each cohort, beginning at
1260 baseline and including assessments post-intervention (at 12 weeks/3 months), and at 9, 12, and
1261 36 months from baseline.

1262

1263 **Primary Research Question and Hypothesis**

1264 Our primary research question is about the impact of the GROW trial on the growth rate of
1265 children’s BMI over time. Specifically, we hypothesize the following:

1266

1267 Hypothesis 1: The BMI trajectories of children in the treatment group will accelerate at a slower
1268 rate than those in the control group over time.

1269

1270 **Primary Outcome**

1271 Although childhood obesity is a well-documented public health concern, most studies have
1272 assessed the obesity outcome (e.g., BMI) using only a single time point or incorporating a pre-
1273 post design, leaving us with little knowledge about the actual shape or growth rate of trajectories
1274 of BMI during this critical period of development. Indeed, few studies have taken a
1275 developmental perspective in order to understand how and when obesity develops in early
1276 childhood. By measuring BMI at multiple time points, we will examine growth trajectories in early
1277 childhood. This will allow us to examine the effect of a prevention program on these varying
1278 trajectories (Agras, Hammer et al. 2004; Pryor, Tremblay et al. 2011). As Barker et al.
1279 demonstrated, it is the change in BMI over time in early childhood, rather than BMI at any one
1280 time point, that is linked with health consequences in adulthood (Barker, Osmond et al. 2005).
1281 Moreover, an earlier childhood adiposity rebound is associated with an increased risk of later
1282 obesity (Rolland-Cachera, Deheeger et al. 1984; Cole 2004). Because clinical literature about
1283 childhood obesity indicates that the shape of the BMI trajectory across ages three to eight is
1284 curvilinear, we will account for this in our analytic plan (Kuczmarski, Ogden et al. 2002; Cole
1285 2004) (see below).

1286

1287 **Primary Analysis**

1288 **Statistical model and approach**

1289 For our primary analysis, which will be an intention-to-treat analysis, we will fit the following
1290 quadratic mixed model equation (some subscripts suppressed for readability):

1291

$$1292 \text{ BMI} = \beta_0 C + \beta_1 I + \beta_2 (\text{age}-X) C + \beta_3 (\text{age}-X)^2 C + \beta_4 (\text{age}-X) I + \beta_5 (\text{age}-X)^2 I + \dots + \text{error terms}$$

1293

1294 where:

- 1295 1. “I” is an indicator for group and equals 1 for the intervention group and 0 for the control
1296 group; “C” is an indicator for group and equals 1 for the control group and 0 for the
1297 intervention group; there is no intercept in this model in the ‘traditional sense’ (see point
1298 two below);

- 1299 2. “X” is the value at which we center age; we plan to use age at enrollment as our
1300 centering term, which will make the indicator variables interpretable (β_0 as the mean BMI
1301 at enrollment for those in the control group and β_1 as the mean BMI at enrollment for the
1302 intervention group);
- 1303 3. “...” stands for other predictors; at the present time, we believe that the predictors for the
1304 main model will be gender (coded, e.g., as 1 for female and 0 for male) and ethnicity (we
1305 expect there to be three ethnicity groups and thus two indicator variables for these); in
1306 addition, gender by age interaction terms will be included, since the literature indicates
1307 that trajectories may differ by gender;
- 1308 4. For the primary analysis, “error terms” will include subject, subject X age, and the
1309 covariance between these random effects, using a heterogeneous variance structure for
1310 the fitted model (Roberts & Roberts, 2005). For the primary analysis, we will not include
1311 a random effect for subject X age², given that, with our proposed unstructured
1312 covariance matrix, the inclusion of this additional random effect would result in 13
1313 random-effects components and may lead to convergence problems (see Rabe-Hesketh
1314 & Skrondal, 2012, page 348). We will examine the consequences of this choice via
1315 planned secondary analyses (see below, section 11.8)
- 1316 5. A post-hoc test of whether will allow us to examine whether the quadratic terms differ
1317 between arms of the trial, thus answering our primary research question.

1318

1319 Interpretation of some terms: the indicator variable for trial arm, the linear term (age) for trial
1320 arm, and the quadratic term (age)² for trial arm jointly describe the trajectory (and starting point)
1321 for each group (intervention and control), and each can be interpreted as follows: the constant is
1322 the mean BMI at age on entry into the trial; the linear term indicates the rate of change at entry
1323 age; and the quadratic term indicates change in rate of growth (acceleration). In our
1324 specification, this model allows each child to have her/his own BMI intercept at baseline and
1325 own BMI trajectory. Accordingly, we do not include BMI at baseline as a predictor in our model.
1326 Additionally, we do not include a BMI by treatment interaction, because BMI is an outcome and
1327 treatment is a predictor. We plan to examine a baseline BMI by treatment interaction (as well as
1328 other interactions) in our secondary analysis (see below).

1329

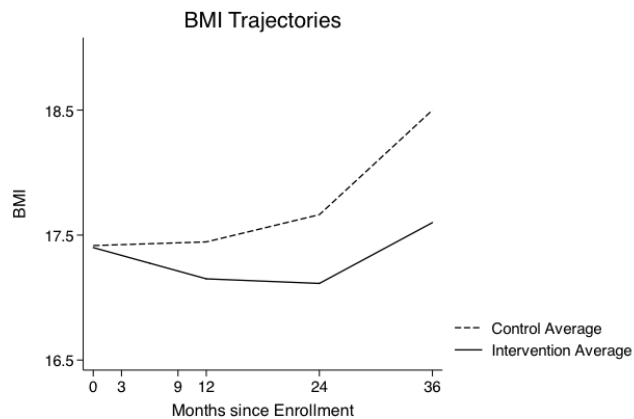
1330 Our hypothesis is that β_5 , the quadratic term for the intervention group, will be significantly
1331 different from β_3 , the quadratic term for the control group, at the 0.05 level. We do not have a
1332 hypothesis about the linear terms. Note that we expect the sign of β_5 to be positive, and we
1333 expect the coefficient to be smaller than the coefficient for β_3 .

1334

1335 A graphical view of the above description is provided below in Figure 11.1 (we have suppressed
1336 the lines for the individual age groups for readability); note that the actual model will produce
1337 smooth curves instead of the piece-wise linear curves shown in the graph.

1338

1339 **Figure 11.1: Projected BMI trajectories over time**



1340

1341

1342 **Assumptions with Justification**

1343 *Assumptions Pertaining to Potential ICC among BMI Trajectories:* We will have three waves of
1344 recruitment with 200 parent-child dyads/wave (100 dyads/arm). The control group will gather in
1345 unchanging groups in local libraries, where we expect little-to-no correlation even though
1346 children will stay in their original session for the entirety of the study. The intervention group
1347 utilizes a social network building component and will have pre-specified parent groups that will
1348 continue throughout the study. The intervention group will attend one of two community
1349 recreation centers (50 dyads/community recreation center/wave). Typically, we will divide these
1350 dyads evenly across three weekly sessions. The session is our subgroup (cluster) of interest.
1351 Each session will have approximately 17 families in it. If the size of the subgroup remains
1352 constant over time, the total number of subgroups we will have is 36, i.e., $600/(50/3)$.

1353

1354 It is also worth noting that we will further subdivide the 17 families of an intervention session into
1355 two smaller subgroups of 8-9 families. This division is done to facilitate our activities and
1356 encourage interaction among these smaller subgroups. It will also likely facilitate the
1357 development of social networks among these groups, which we hypothesize to be related to
1358 improved health outcomes for the treatment group over the course of our intervention. If we take
1359 this smaller subgroup as the unit for the intervention group, our total number of subgroups is 54,
1360 i.e., $18+36$, or $[300/(50/3)]+[300/(50/6)]$, where the first square bracket is the number of
1361 subgroups in the control group (where subgroups are not broken down into smaller subgroups),
1362 and the second square bracket is the number of subgroups in the intervention group.

1363

1364 The social networking aspect within the intervention group and the smaller group size lead us to
1365 predict a positive but small ICC that may be higher than what we expect to be a small ICC in the
1366 control group. Note, however, that session membership is well-defined for both the intervention
1367 arm and control arm, as participants will have minimal movement between sessions. This leads
1368 us to propose a heterogeneous variance structure for the primary analysis, allowing the ICC at
1369 the level of session to be estimated separately for the intervention and control arms.

1370

1371 Checking and Sensitivity Analyses: Once a model has been estimated, we will need to
1372 investigate its properties not only to ensure that any data idiosyncrasies do not impact the
1373 results but also to help ensure that the results are generalizable. The first issue is to check for
1374 systematic differences between the model and the data using graphs, such as comparisons of
1375 predicted and observed values of BMI, and other standard diagnostics (Snijders 2008). An
1376 extension of this idea is to simulate new sets of outcomes, based on our model, and use the
1377 simulated data as a reference test group by comparing this set to the observed result; in this
1378 case, we would look for situations in which the data appear different from what we would expect
1379 by using the model to predict the data (Gelman 2007).

1380

1381 A second issue is whether we have left out important features of the model, including, for
1382 example, (1) age at randomization, (2) measurement occasion, (3) study wave (by which we
1383 mean enrolled in first year, second year, or third year of the program), or (4) other demographic
1384 variables (e.g., SES, parent level of education) or substantive covariates (e.g., maternal
1385 depression). Some of these variables will be tested explicitly as moderators or mediators (see
1386 previous sections pertaining to moderators and mediators as well as sections 11.6 and 11.7
1387 below). In addition, trajectories may vary by baseline BMI; this possibility will be checked by
1388 estimating a model with a baseline BMI by treatment group interaction. We will estimate
1389 additional models that include one or more of these additional features to check whether
1390 inclusion of any of these predictors is both statistically reasonable and affects our conclusions.

1391

1392 A third issue is whether age is correctly specified. With six data points, a limit exists as to what
1393 can reasonably be done. We suggest that the quadratic model should be checked in two ways:
1394 (1) substitute linear splines with a break between, for example, ages 4 and 5 (anticipated
1395 adiposity rebound timing); (2) substitute non-linear splines, in particular, restricted cubic splines
1396 with 4 knots chosen following Harrell's default positions (Harrell 2001).

1397

1398 A fourth issue relates to the potential correlation among the clusters/subgroups in our analysis:
1399 to what extent are these clusters correlated, what is the effect of that correlation on our results,
1400 and how accurately have we specified the clusters? Although we will not use the cluster-
1401 adjusted robust sandwich estimator in our primary analysis, we will, as a safeguard, fit a model
1402 that assumes a cluster structure within the data and compare the standard errors of this model
1403 to those from our primary model. If there are substantive changes in the standard errors, further
1404 work will be done to see which set of standard errors is more appropriate in our situation.

1405

1406 **Missing data including level of attrition, lost to follow-up, and missing data treatment**

1407 Estimated Attrition: Within each planned cohort of 200 dyads per three cohorts, six waves of
1408 data collection will occur, with shorter time intervals between the earlier waves and longer time
1409 intervals later. According to prior community-based studies, subject dropout decelerates over
1410 time, with the worst losses occurring early. We will make every effort to reduce attrition, with
1411 particular focus on the earlier waves of the study, to ensure that we retain at least 80% of our
1412 sample within each cohort, yielding a cohort size of at least 160 and a total sample size, at
1413 study end, of at least 480. This level of attrition would leave us sufficiently powered (.90) to be

1414 able to detect a standardized effect size of .40 (a respectable and common effect size unique to
1415 the analytic method we are using--see sample size and power analysis section). An even larger
1416 sample size will increase the power to detect a meaningful difference, as explicated in the
1417 power analysis and sample size section below, and we will strive to ensure that the sample is as
1418 large as possible at each successive wave. In addition, it is important to note that our analysis is
1419 an intention-to-treat analysis. Accordingly, we will use all cases in our analyses, even those with
1420 as few as one wave of data, such that attrited cases will not truly be lost but instead retained in
1421 our analytic procedures.

1422

1423 Missing Data: Conceptually, we anticipate two types of missing data: (1) people who drop out
1424 after a measurement occasion and never return [i.e., lost to follow up]; and (2) people who miss
1425 one or more particular measurement occasions (e.g., occasion three) but are present for each
1426 of the others, at least one of which is later in time than the one (or more) that they missed.

1427

1428 With six repeated measurements, some participants inevitably will miss one or more occasions
1429 of outcome data collection. One advantage of the mixed models over older repeated measure
1430 ANOVA models is the use of all available data without dropping any subjects (Nich and Carroll
1431 1997). We begin by assuming that the missing occasions meet MCAR or MAR assumptions
1432 (Little and Rubin 2002). If so, the results of the mixed model (e.g., the effect of time, group by
1433 time) are robust.

1434

1435 To guard against missingness biasing results, we will also conduct secondary analyses of
1436 missingness to see how realistic the assumption of MAR or MCAR may be. This check can be
1437 done in several ways. We will start with descriptive statistics comparing the characteristics of
1438 observations with and without missing values (e.g., gender, baseline BMI, age at enrollment,
1439 etc.). The first analysis will use standard multiple-imputation with 100 imputations (Little and
1440 Rubin 2002). Three possible directions, in addition to standard diagnostics (White, Royston et
1441 al. 2011) can be pursued when checking whether being missing is non-random (i.e., in checking
1442 the results of the multiple imputation):

1443

1444 1) The first method is our primary suggestion: we will impute the data using standard
1445 multiple imputation (MI) software but with constraints on the values that can be imputed.
1446 These constraints arise because our prime concern regarding non-random missingness
1447 is that either those who don't need the program (i.e., those who are lean) or those who
1448 perceive that they are not seeing an effect (i.e., who are, and remain, overweight) will
1449 miss occasions. For example, in one set of imputations we would constrain all imputed
1450 BMIs to be below, say, "a"; in a different set, we would constrain the imputed BMIs to be
1451 above, say, "b"; this type of constrained MI is discussed in An and Little(An, Little et al.
1452 2010) and Jenkins, Burkhauser, Feng, and Larrimore(Jenkins, Burkhauser et al. 2011).
1453 One hundred imputations will be used for each such constrained MI. We will examine
1454 the BMI pattern of those who drop out and, if we see evidence of either "a" or "b", use
1455 the values we observe to set the constraints.

1456 2) A second possible type of sensitivity analysis was originally suggested by Rubin (1987)
1457 and has been extended by Carpenter, Kenward, and White,(Carpenter, Kenward et al.

1458 2007) who suggest weighting each imputed result (rather than Rubin's standard simple
1459 averaging of the results), where the weight depends on the assumed departure from the
1460 MAR assumption. Their technique relies on at least one strong assumption, but they
1461 provide a graphical diagnostic to help check this assumption.

1462 3) If drop-outs (situation one above) are much more common than missing an occasion and
1463 then returning (situation two above), we will estimate a pattern-mixture model (Little
1464 1993; Hedeker and Gibbons 1997). If missing one or more occasions and then returning
1465 is relatively common, however, we will not pursue this strategy.

1466

1467 **Detectable Difference, Sample Size, and Power**

1468 Power and Sample Size Estimation: The power analysis was performed on our primary analysis
1469 (see below): a quadratic model of the BMI trajectories. For our sample size estimation, we used
1470 the OD (Spybrook 2011) software so that we would be consistent with our planned analysis.
1471 This software allowed us to examine two-group repeated-measures trials with quadratic change,
1472 the same model being used for the analysis.

1473

1474 This software uses a standardized effect size as defined in Raudenbush and Liu, namely, the
1475 group difference on the polynomial trend divided by the "population standard deviation of the
1476 polynomial trend of interest" (p. 391; the "population standard deviation" refers to the square
1477 root of the variance of the random effect) (Raudenbush and Xiao-Feng 2001). This specification,
1478 particularly the denominator, is quite different from cross-sectional standardized effect sizes
1479 such as Cohen's D, given that, with a polynomial model (here quadratic), the difference between
1480 groups depends on the point in time examined. In particular, given our hypothesis (see below),
1481 we expect that, after adiposity rebound is reached, the BMI of children in the intervention group
1482 will grow more slowly than that of children in the control group such that the differences between
1483 their mean BMIs will increase over time. Our expectation implies that we are interested in the
1484 significance of the quadratic term in the model, and expect that the difference between the
1485 control and treatment group quadratic effect will be significantly different from zero.

1486

1487 We note one difference between the OD program's assumptions and our study: the OD program
1488 assumes that the measurement occasions will be equally spaced over time, which is not the
1489 case in our study. As a result, specifications from the OD program may lead us to overestimate
1490 power and underestimate sample size. Power is high in the current study, as can be seen in the
1491 table below, thus we expect that these potential mis-estimations are not problematic.

1492

1493 To determine the power and effect size of the current study, we need estimates of the
1494 standardized effect size, which we obtained from a subset of our previous Salud Con La Familia
1495 study. We used only a subset of the Salud subjects because the inclusion criteria for that study
1496 (i.e., children at any level of baseline BMI) were broader than for the current study (i.e., children
1497 whose baseline BMI is between the 50th and 95th ([or 99th] percentile). For our estimations, then,
1498 we used only the Salud data for those from the 50th to the 95th percentile (and then again from
1499 the 50th to the 99th percentile [see below]). Other important differences exist between Salud and
1500 the current study, however, that limit our ability to estimate power and sample size based solely

1501 on Salud: (1) the Salud subjects had only three measurement occasions which covered 15
 1502 months rather than six occasions over three years (the GROW trial) and (2) the Salud
 1503 intervention was comparable only to the 12-week intensive phase proposed in the GROW study
 1504 and did not include a maintenance or sustainability phase as proposed in the GROW trial. We
 1505 expect that the increased number of sessions as well as the intensity of the intervention in the
 1506 GROW trial will serve only to increase the power of the GROW study.

1507
 1508 When using the OD software, the user can set various values, the most important of which is
 1509 the standardized effect size discussed above. Other possible values to set include the duration
 1510 of the study (here, three years), the number of measurement occasions (here six), and the
 1511 variance of the residuals and the variance of the random effects. We found that even fairly
 1512 sizable changes in value used for the residuals and the variance of the random effects had little
 1513 effect on the projected sample size (e.g., holding other elements constant and changing the
 1514 variance of the random effect of age-squared from the observed standard deviation of 2.8
 1515 [based on the Salud data] to the OD program's default of 1, only increased the sample size at a
 1516 power of 0.8 by about 20 subjects). Using the program defaults for residuals and variance of the
 1517 random effects was a conservative (i.e., produced larger estimates of sample size) approach
 1518 compared to using the results based on Salud, thus we used these defaults in the table below.
 1519 Changing the standardized effect size does have important consequences for the estimated
 1520 sample size, however (see Table 9).

1521
 1522 As previously stated, we used the Salud data to estimate our primary model (see below) for
 1523 those within that study who were between the 50th and 95th BMI percentiles at baseline. The
 1524 control group in the Salud data showed unexpected results with virtually no non-linearity (i.e.,
 1525 their BMI trajectories increased but in a linear fashion over a 15 month period), therefore we
 1526 believe that the effect size from that model, which was quite large and based on different
 1527 assumptions, is an overestimate of the effect that we will see in the GROW study. Instead we
 1528 used the OD program default for the effect size of 0.4, a commonly used effect size in
 1529 longitudinal studies and thus the OD program default, to estimate our required sample size.
 1530 Accordingly, Table 9, below, indicates, for powers of 0.7, 0.8, and 0.9, the estimated sample
 1531 size using the OD program for the default effect size (0.4) and for two additional effects sizes, a
 1532 smaller and more conservative effect size (0.3) and a larger and more liberal effect size (0.5).
 1533 As the table below indicates, we estimate that recruiting a sample size of at least 480 will leave
 1534 us adequately powered to determine this middle/medium effect size of 0.4.

1535
 1536 **Table 9: Estimated required sample size for given standardized effect sizes**

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

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

1537

1538 Because the results of our pilot study currently underway have led us to consider including
 1539 children with higher baseline BMI in the GROW trial than we had originally planned, we also
 1540 estimated our primary model on Salud participants who were between the 50th and 99th
 1541 percentile of baseline BMI to determine the effects of including these children with a higher BMI.
 1542 While, as expected, the variance increased when we moved to the model that added children
 1543 between the 95th and 99th percentiles, the difference between groups (control and intervention)
 1544 also increased such that the standardized effect size changed very little and, thus, there was
 1545 virtually no effect on power (i.e., the desired sample size, under various conditions, never
 1546 changed by more than two people). If, then, we decide to extend our criteria in the GROW trial
 1547 to include children who are in the 95th to 99th percentile of BMI at baseline, our analyses will
 1548 continue to be sufficiently powered.

1549

1550 Currently, the design for the GROW trial includes 600 children, and, though we would expect to
 1551 be adequately powered at a smaller number of subjects, we plan to recruit 600 subjects to allow
 1552 for potential attrition. We note, however, that if recruitment of that higher number of subjects
 1553 becomes problematic (and we have observed in our current pilot study the difficulties inherent in
 1554 recruitment for a similar prevention trial), we will stop subject recruitment at a smaller number of
 1555 subjects, though ideally not less than 480 (see Table 9), such that we are adequately powered.

1556

1557 **Analysis for Possible Effect Modifiers**

1558 The variables that are listed in the previous section as moderators (e.g., race/ethnicity, genetic
 1559 risk score, etc.) will be entered appropriately into the analytic model as interaction terms in order
 1560 to test the effect of the moderator on the outcome (child BMI trajectory). Relevant three-way
 1561 interactions (e.g., child gender by age by group) will also be tested.

1562

1563 **Analysis for Possible Effect Mediators**

1564 The variables that are listed in the previous section as mediators/covariates will be entered into
 1565 the analytic model as time-varying covariates and their effects on the outcome will be assessed
 1566 accordingly, controlling for all else in the model.

1567

1568 **Secondary Hypotheses and Analysis**

1569

1570 Secondary Analyses: We list below two sets of secondary analyses. The first is specific to our
 1571 primary analysis (see Aim 1, Hypothesis 1); the second is specific to the secondary aims and
 1572 related hypotheses (see Aims 2-6) and contained under section 11.9 (below).

1573

1574 **Secondary Analyses in relation to the Primary Hypothesis and Analysis**

1575

1576 1) Timing of adiposity rebound: We anticipate that we will be able to characterize and
1577 capture the timing of adiposity rebound for many of the children enrolled in the study. At
1578 time of enrollment, each child is at least three years of age and is less than six years of
1579 age (and we will know, including fractions, how old they are at enrollment by collecting
1580 their date of birth); measurement occasion six will occur at least three years after
1581 enrollment. Using these conditions, those who enroll on their third birthday will be at
1582 least six years old at measurement occasion six (and everyone else will be older); in this
1583 scenario it is reasonable to assume that most subjects who enroll at age three will have
1584 reached adiposity rebound by measurement occasion six, although we will miss some
1585 children who have earlier/later rebound timing. Also, virtually all children who enroll at
1586 age four should experience adiposity rebound during the study, but a few might be
1587 earlier than four or later than seven. Finally, the majority of those who enroll at age five
1588 should experience adiposity rebound during the study, but a minority will have
1589 rebounded prior to age five. Note that the mean age at adiposity rebound is a simple
1590 function of the coefficients from the main model: $-\beta_2/(2*\beta_3)$ will be the nadir for the control
1591 group (and a similar calculation captures the intervention group:

1592 $-\beta_4/(2*\beta_5)$).

1593 2) The effect of parental change in BMI over the study period on child's growth trajectory: In
1594 this study, this effect will be modeled by including baseline BMI of the parent as a
1595 predictor, and also including other measures of parent BMI as time-varying covariates
1596 (i.e., the value of the covariate depends on the measurement occasion).

1597 3) We will test the difference between mean BMI for both groups at the end of the trial (36
1598 months) to determine whether they are significantly different from one another, thus
1599 adding additional information to our analyses.

1600 4) We will test whether the trajectories of both normal and overweight children in the
1601 treatment group accelerate at a slower rate than those in the control group over time,
1602 such that those in the treatment group will be less likely to evidence trajectories of
1603 obesity compared to those in the control group. Each child will be categorized as having,
1604 or not having, an acceptable BMI trajectory. This binary variable will be the outcome
1605 variable for this secondary analysis. We will test this first, in an unadjusted analysis (a 2
1606 by 2 table where one variable is the outcome variable and the other is group [control or
1607 treatment]), and then in an adjusted analysis using logistic regression. Predictors in the
1608 logistic regression will include demographics (e.g., gender) and various baseline
1609 variables, including the baseline BMI weight category (i.e., normal or overweight).

1610 5) In a series of secondary analyses, we will examine the random-effects in more detail:

1611 1. Using our original fitted model, we will impose an independent covariance matrix
1612 (which assumes no correlation between random effects), reducing the resulting
1613 number of random effects from seven to five. The results of this change to the model
1614 will inform us about the next two steps (see below).

1615 2. We will add the two age-squared terms (for intervention and control) as random
1616 effects, continuing to use the independence structure, and bringing the number of
1617 random effects back to seven.

- 1618 3. Keeping the two age-squared terms as random effects, we will return to an
1619 unstructured covariance matrix, bringing the number of random-effects to 13.
- 1620 4. At each step in the above process, we will evaluate the results of continuing to add
1621 additional random effects terms, including noting model convergence problems.
1622 While we believe the model with 13 random effects will have reduced power and thus
1623 do not propose this model for our primary analysis, we believe that fitting this model
1624 in a secondary analysis, via the systematic steps outlined above, will allow us to
1625 examine the consequences of including a large number of random effects and
1626 determine the viability of this alternate model.
- 1627 5. It is possible that in addition to different ICC's per condition, variability may occur
1628 across sessions within condition, such that a range of ICCs exists. If that range is
1629 determined to be sufficiently wide, we will consider adding cluster-adjusted standard
1630 errors for both the fixed and random-effects. Note that this type of standard error is a
1631 generalization of the traditional sandwich estimator; StataCorp has provided a FAQ
1632 on this generalization with citations:
1633 http://www.stata.com/support/faqs/stat/robust_ref.html.

1634

1635 **Additional Analyses**

1636

1637 **Secondary Analyses in relation to the Secondary Aims and Hypotheses**

1638 In addition to the above analyses, we will conduct analyses necessary to support our secondary
1639 aims of the trial, as outlined below.

1640

1641 **Aim 2: Compare the effect of the intervention in children who made significant changes 1642 in their dietary and/or physical activity behaviors to the effect in children who did not.**

1643 Hypothesis 2: Relative to children in the control condition, children participating in the treatment
1644 condition will:

1645 2.1 Have lower sedentary activity levels (as measured by actigraphy data) after the intensive
1646 phase of the intervention (T2) and at study completion and/or

1647 2.2 Have better adherence to age-specific USDA nutrition recommendations, (e.g., age-
1648 appropriate total calories increased, fruits and vegetables, decreased sugar sweetened
1649 beverages [measured via diet recall data]), after the intensive phase (T2) and at study
1650 completion.

1651

1652 **Analysis:**

1653 **(2.1)** A multiple regression model in which child sedentary activity level is regressed on group,
1654 controlling for baseline sedentary activity level and including other relevant covariates (e.g.,
1655 child gender), will be fit at T2 and at study completion.

1656 **(2.2)** Each child will be categorized as evincing, or not evincing, adherence to age-specific
1657 USDA recommendations (as defined in the hypothesis). This binary variable will be the outcome
1658 variable for this secondary analysis. We will test this first in an unadjusted analysis (a 2 x 2 table
1659 in which one variable is the outcome variable and the other is group [treatment or control]), and

1660 then in an adjusted logistic regression analysis predicting adherence category membership and
1661 including appropriate covariates (e.g., gender, baseline BMI) in addition to group.

1662

1663 **Aim 3: Evaluate the effect of parents' physical activity levels and dietary behaviors on**
1664 **children's levels of the same.**

1665 Hypothesis 3: Parents who have significantly lower sedentary activity levels (compared to
1666 baseline) after treatment or who have better adherence to USDA nutrition recommendations
1667 (age-appropriate total calories increased fruits and vegetables, decreased sugar sweetened
1668 beverages [measured via diet recall data]) will be more likely than parents who have higher
1669 sedentary activity levels or who do not adhere to USDA nutrition recommendations to have
1670 children who will show

1671 3.1: Decreased sedentary activity levels post-treatment and

1672 3.2: Better adherence to USDA nutrition recommendations (as measured in 2.2, above).

1673

1674 **Analysis:**

1675 Two binary predictors will be created denoting whether parents have significantly lower
1676 sedentary activity compared to baseline (yes/no) and whether they have appropriate versus
1677 inappropriate dietary adherence (yes/no). These dichotomous variables will be entered into
1678 models as follows:

1679 **(3.1)** A multiple regression model will be fit at T2 and at study completion in which child's
1680 sedentary activity level is regressed on group, controlling for baseline child sedentary level, and
1681 including the parent dichotomous variables, and two two-way interactions between the parent
1682 variables and group (treatment or control) (and including other relevant covariates [e.g.,
1683 gender]).

1684 **(3.2)** A logistic regression model will be fit at T2 and at study completion in which the binary
1685 child adherence variable (see hypothesis 2.2) is regressed on group and including the parent
1686 dichotomous variables and two two-way interactions between the parent variables and group
1687 (treatment or control)

1688 (and including other relevant covariates [e.g., gender]).

1689

1690 **Aim 4: Explore the potential for developing new social networks and their effect on child**
1691 **nutrition and physical activity.**

1692 Hypothesis 4: Parents in the treatment group will develop new social networks and the strength
1693 of those social networks will be positively associated with reduced sedentary activity levels and
1694 improved dietary behaviors (measured as indicated above) among both parents and children.

1695

1696 **Analysis:**

1697 A social network analysis will be conducted to determine the strength and cohesion of parents'
1698 reported networks. The effect of these networks on parental and child sedentary activity levels
1699 and dietary behavior will be estimated. Social network analysis will be conducted using the

1700 software packages UCINET and In-Flow. UCINET will be used for entering and analyzing
1701 network data and, along with In-flow, for generating network measures and graphical displays.
1702 This data set will thus contain both network and attribute variables at the individual level of
1703 analysis. Applying standard statistical techniques (e.g., regression, logistic regression, etc.)
1704 these independent variables will be modeled with selected dependent variables. The analysis
1705 will examine the change in these social networks over time and their impact on the main
1706 outcomes of interest including: growth trajectories (children's BMI); body composition (child and
1707 adult), parenting practices (child feeding); physical activity (child and adult), and total energy
1708 intake. The social network hypothesis suggests that members of a given network group will
1709 share health behavior characteristics more than members of other groups.

1710

1711 **Aim 5: Evaluate the moderating relationship between genetic risk factors and child BMI**
1712 **trajectories over the course of the study.**

1713 Hypothesis 5: Higher levels of child genetic susceptibility to obesity (i.e., a higher genetic risk
1714 score (Kathiresan, Voight et al. 2009)) will be significantly associated with heavier-for-age BMI
1715 at baseline, and this susceptibility will moderate children's growth in BMI over time.

1716

1717 **Analysis:**

1718 "Heavier-for-age-BMI at baseline", the outcome, will be regressed on genetic risk score and the
1719 interaction between risk score and time, controlling for other covariates as deemed important
1720 (e.g., child gender, etc.).

1721

1722 **Aim 6: Assess the degree to which implementation of the GROW program encourages**
1723 **additional lifestyle programming for preschool children and their parents in the Metro**
1724 **Community Centers.**

1725 Hypothesis 6: The two Metro Community centers participating in the GROW trial will implement
1726 a higher number of activity or nutrition programs for families (as defined by the centers) with
1727 young children at the end of the study compared to the number they implemented at baseline,
1728 and they will also implement a higher number after the study compared to the number
1729 implemented by non-participating Metro Community Centers.

1730

1731 **Analysis:**

1732 A simple count of the number of activity and nutrition programs will be taken at baseline within
1733 both Community Centers (i.e., East and Coleman) and then again at the end of the study to
1734 determine whether the number at study end within each center exceeds that at baseline.
1735 Similarly, counts will be taken of these types of programs at non-participating Metro Community
1736 Centers at baseline and study end and these numbers will be compared to counts at both East
1737 and Coleman to determine if both participating centers have higher numbers than the non-
1738 participating centers at baseline and at study end.

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1921 **Revised Protocol**

1922 **Specific Aims**

1923 This research includes one primary and five secondary specific aims:

1924

1925 Primary Aims:

- 1926 1. **Aim 1:** Evaluate the efficacy of a multi-level intervention, addressing nutrition and
1927 physical activity, at public community recreation centers with high-risk parent- preschool
1928 child (ages 3-5) dyads to promote pediatric obesity prevention.
1929 1.1. **Hypothesis 1:** The BMI trajectories of children in the treatment group will accelerate
1930 at a slower rate than those in the control group over time.

1931

1932 Secondary Aims:

- 1933 2. **Aim 2:** Compare the effect of the intervention in children who made significant changes
1934 in their dietary and/or physical activity behaviors to the effect in children who did not.
1935 2.1. **Hypothesis 2:** Relative to children in the control condition, children participating in
1936 the treatment condition will:
1937 2.1.1. Have lower sedentary activity levels (as measured by actigraphy data)
1938 after the intensive phase of the intervention (T2) and at study completion and
1939 2.1.2. Have better adherence to age-specific USDA nutrition recommendations,
1940 (e.g., age-appropriate total calories increased fruits and vegetables, decreased
1941 sugar sweetened beverages [measured via diet recall data]), after the intensive
1942 phase (T2) and at study completion.
1943
1944 3. **Aim 3:** Evaluate the effect of parents' physical activity levels and dietary behaviors on
1945 children's levels of the same.
1946 3.1. **Hypothesis 3:** Parents who have significantly lower sedentary activity levels
1947 (compared to baseline) after treatment and who have better adherence to USDA
1948 nutrition recommendations (age-appropriate total calories increased fruits and
1949 vegetables, decreased sugar sweetened beverages [measured via diet recall data]) will
1950 be more likely than parents who have higher sedentary activity levels and who do not
1951 adhere to USDA nutrition recommendations to have children who will show
1952 3.1.1. Decreased sedentary activity levels post-treatment and
1953 3.1.2. Better adherence to USDA nutrition recommendations
1954
1955 4. **Aim 4:** Explore the potential for developing new social networks and their effect on child
1956 nutrition and physical activity.
1957 4.1. **Hypothesis 4:** Parents in the treatment group will develop new social networks and
1958 the strength of those social networks will be positively associated with reduced
1959 sedentary activity levels and improved dietary behaviors (measured as indicated above)
1960 among both parents and children.
1961
1962 5. **Aim 5:** Evaluate the moderating relationship between genetic risk factors and child BMI
1963 trajectories over the course of the study.
1964 5.1. **Hypothesis 5:** Higher levels of child genetic susceptibility to obesity (i.e., a higher
1965 genetic risk score)⁹ will be significantly associated with heavier-for-age BMI at baseline,
1966 and this susceptibility will moderate children's growth in BMI over time.
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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.

2006 Changes in physical activity and diet, among many other factors, have contributed to epidemic
 2007 levels of childhood obesity in the U.S.¹⁻⁵ Obesity rates have tripled among children and
 2008 adolescents over the past thirty years^{6,7}, with Latino and African-American populations at
 2009 disproportionately higher risk.^{3,7,8} At the current rates of childhood obesity, 30 to 40% of today's
 2010 children may eventually develop type 2 diabetes and reduce their life expectancy.⁹ Nader et al
 2011 demonstrated that children who were ever overweight during the preschool period were five
 2012 times as likely to be overweight adolescents.¹⁰ And the chances of overweight increases as the
 2013 child ages. In that same study, 80% of school-age children who were ever overweight during
 2014 this period went on to become overweight adolescents. The significance of mounting risk for
 2015 sustained overweight and its consequences cannot be overstated. In the Harvard Growth Study,
 2016 overweight adolescents as adults had a two-fold increase in all-cause mortality and an

2017 increased morbidity due to cardiovascular disease.¹¹ It is not merely overweight/obesity in
2018 childhood that poses the risk for later increased mortality and morbidity as an adult, **the slope**
2019 **of early weight gain is a potent predictor.**^{12,13} For example, Leunisson et al showed that rapid
2020 weight gain without concomitant growth in height during the first three months of infancy is
2021 linked with reduced insulin sensitivity in early adulthood. **Furthermore, Barker et al**
2022 **demonstrated that the risk of adult coronary events was more strongly related to the**
2023 **rapid childhood gain in BMI than to BMI attained at any particular age.**¹² **Consequently,**
2024 **this proposal will address prevention of rapid BMI gain during early childhood, fostering**
2025 **normal growth for those children who have a normal BMI (>50% and <85%) and**
2026 **improving BMI trajectories for those children who already have a BMI ≥ 85% <95% at**
2027 **ages 3-5 years.** There is little evidence documenting successful behavioral interventions to
2028 *prevent* early childhood obesity¹⁴⁻¹⁶ and even less evidence concerning which factors may be
2029 crucial to success. Consequently, the Institute of Medicine (IOM)^{17,18} and the *Strategic Plan for*
2030 *NIH Obesity Research*^{19,20} call for a community-engaged, culturally-relevant, family-centered
2031 approach to obesity prevention that can be sustainable.

2032

2033 ***Family plays a crucial role in pediatric obesity prevention.***

2034 Family influences normative expectations of how and what to eat as well as how often to be
2035 physically active.^{21,22} Moreover, families control the home environment that shapes children's
2036 early childhood choices, establishing behavioral habits.²³ For example, in the Viva La Familia
2037 study, random 24-hour dietary recalls of almost 1000 children showed that 67% of children's
2038 meals occurred at home and that most of these meals were high density, low nutrient foods,
2039 consistent with their parents' choices.²⁴ Parental involvement in programs to reduce overweight
2040 in children has been moderately successful, and is considered an important component of
2041 weight loss programs targeting children.^{25,26} Many of these programs were focused on
2042 treatment, however, the same association appears to exist for prevention efforts as reported in a
2043 recent meta-analyses of randomized trials to prevent childhood obesity.²⁷ Parents' role appears
2044 to be as both models to their children and as active participants in creating a healthy
2045 environment that encourages healthy lifestyles. Children are nearly six times more likely to be
2046 physically active if their parents are physically active.²⁸

2047 One important component of parental involvement is the use of behavior change methods such
2048 as parent-child contracting to set clear goals for nutrition and activity and self-monitoring of
2049 caloric intake and activity.^{26,29} Epstein's report of 10-year treatment outcomes for obese children
2050 indicates long-term success among families who used parent-child contracts to set clear
2051 goals.²⁶ In a 2006 position paper, the American Dietetic Association (ADA)^{30,31} recommended
2052 that effective, developmentally appropriate pediatric obesity interventions include the following
2053 elements:

- 2054 1) Parent training/modeling (involving behavioral counseling targeted at parents to improve their
2055 parenting skills);
- 2056 2) Behavior modification training (involving goal setting, modeling, and self-monitoring);
- 2057 3) Promotion of physical activity (including the reduction of sedentary behaviors); and
- 2058 4) Nutrition counseling/education (including the provision of more general information on foods,
2059 shopping, and nutrition to promote healthful eating).

2060

2061 ***Obesity is impacted by both the physical and social environment.***

2062 It is not only the family that exerts influence over preschooler nutrition and physical activity
2063 habits, but both the physical and social environment.

2064 ***Physical Environment:*** A developing area of research examines the impact of access to physical
2065 activity on increased activity levels. In a study by Wilson et al, access to physical activity such
2066 as neighborhood trails was associated with increased physical activity in low SES groups.³²
2067 These same groups tend to have a higher likelihood of obesity.³³ Likewise, Sallis et al
2068 discovered that proximity of exercise facilities to one's home was associated with increased
2069 amounts of exercise.³⁴ Unfortunately, more physical activity barriers exist for residents living in
2070 poorer communities. For example, Estabrooks found that fewer free physical activity resources,
2071 such as parks and playground exist, in poorer communities.³⁵ Lack of affordable, safe, and
2072 accessible recreation facilities and programs have been cited as contributing to children's
2073 watching more TV at home, which in turn is associated with increased rates of obesity.^{4,36}
2074 Creating links to free, accessible recreation would be especially important in areas where low
2075 SES populations live. **Public community centers provide access to physical activity for
2076 those populations at highest risk for obesity. Through our existing partnership between
2077 the Department of Pediatrics at Vanderbilt University Medical Center (VUMC) and Metro
2078 Parks and Recreation, we have the opportunity to conduct and test a community center
2079 based intervention that can reach this high risk population.**

2080 ***Social Environment:*** Research now suggests that we have underestimated the influence of the
2081 social environment on shaping obesity-related behaviors. Social networks have been linked to
2082 obesity in adults and adolescents.³⁷⁻⁴⁰ From a recently completed afterschool intervention
2083 (Gesell PI), we have initial support for our approach to spread physical activity through a newly
2084 developed network. Results indicated that children's existing friendships heavily influenced their
2085 routine level of physical activity. The strongest influence on the amount of time children spent in
2086 moderate-to-vigorous activity in the afterschool hours was the activity level of their immediate
2087 friends. Children consistently made adjustments to activity levels of 10% or more in order to
2088 emulate the activity levels of their peers (OR=6.89, p<.01). The child's own age (OR=.92, p<.10)
2089 and obesity status (OR=.66, p<.10) had statistically significant but relatively small direct effects
2090 on the individual's activity level. Gender had no direct effect on activity.⁴¹ In another recently
2091 published study, we found that a new social network evolved among parents enrolled in a
2092 community-based obesity prevention RCT: Parents selectively formed friendship ties based on
2093 child BMI z-score, ($t=2.08$, $p<.05$), thus revealing the tendency for mothers to form new
2094 friendships with mothers whose children have similar body types.⁴² Together, this work supports
2095 our proposition of utilizing the social influences of social networks that form during our
2096 intervention to amplify obesity-preventing behavior change. In the GROW intervention we will
2097 build new social networks through: frequent contact and facilitated interaction in structured small
2098 group activities.

2099 Although the terms are often used interchangeably, social networks differ from social support.
2100 Social networks, the complex webs of social relationships and social interactions that connect
2101 individuals, have been shown to be strong influences on behaviors. Social support, however, is
2102 generally thought not to influence behavior, but rather be a mechanism to cope with challenges
2103 and facilitate recovery from illness, injury or disease.⁴³ Methodologically, social support is
2104 measured from the respondent's perspective to assess the support (e.g., emotional, cognitive,
2105 tangible support) an individual perceives to have, whereas social networks typically measure the

2106 presence or absence of friendships and task- or work-oriented relationships (which may or may
2107 not provide support) and treats the ties themselves as objects of study.⁴⁴ Social network
2108 analysis allows us to see the whole group of individuals and their interconnectedness, and is in
2109 that sense broader than analysis of social support. Due to a dearth of data and to
2110 methodological challenges, there are fewer studies of how social networks affect health.

2111
2112 ***Genetic factors play a role in the development of obesity.***

2113 New research demonstrates a genetic risk score (GRS) is a potent predictor of BMI.
2114 Family studies have demonstrated that genetic factors account for anywhere between 40% and
2115 70% of the population variance in BMI for individuals with severe obesity.^{45,46} Until recently,
2116 specific genes contributing to BMI in the general population had not been identified. It is now
2117 clear, however, that certain gene variants exert a substantial, clinically important effect on BMI
2118 in humans.⁴⁷ The GIANT Consortium recently reported the results from large scale studies to
2119 identify genetic variants contributing to the risk of obesity in both children and adults. In January
2120 2009, this consortium reported a meta- analysis involving over 100,000 patients, in which 8
2121 obesity-related risk alleles were conclusively validated far in excess of the standard (5 x 10⁻⁷)
2122 for genome-wide statistical significance.⁴⁷ Moreover, whereas each particular obesity
2123 susceptibility variant confers only a modest effect on BMI, a genetic risk score summing each
2124 individual's number of susceptibility variants across all 8 genes is a more potent predictor of
2125 obesity.⁴⁷ All of the genes are on different chromosomes (unlinked), and therefore, were treated
2126 as an independent variable. Given that humans have two copies of every autosomal gene,
2127 each person has 0, 1, or 2 risk alleles at each locus, with a genetic risk score (GRS) ranging
2128 from 0-16 (for 8 genes, given 2 alleles per locus, maximum score is 16). Even in the general
2129 population, at the extremes of GRS, BMI ranges from 25- 27 are clearly associated with clinical
2130 obesity. A novel aspect of the present proposal is that it incorporates genetic data in relation to
2131 an interventional study to prevent early childhood overweight/obesity. It has now been
2132 conclusively demonstrated that specific genes predispose to obesity, yet their impact on early
2133 obesity prevention has not been studied. This critical question must be answered in order to
2134 translate the findings of genetic studies effectively into clinical practice.

2135
2136 Prevention must occur in preschool given that 60% of overweight preschoolers will go on to
2137 become overweight adolescents.¹⁰ By conducting and testing trials in public community
2138 centers, exportable interventions could result allowing for a macro-level system change to
2139 address this expanding public health crisis. **Building on the success of an existing
2140 partnership between Vanderbilt Pediatrics and Metro Parks and Recreation in Nashville,
2141 TN, the team in this proposal will conduct and evaluate an intervention intended to
2142 prevent obesity in preschoolers in an approach that affects multiple levels of risk and is
2143 both family-based and community-centered. This research includes the following
2144 innovations:**

- 2145 1. Evaluates the trajectory of early BMI gain, as directed by recent scientific discoveries.^{12,13,48}
- 2146 2. Conducts a pediatric obesity prevention trial based in public community centers that are
2147 routinely available to the populations at highest risk.
- 2148 3. Addresses obesity in the understudied period of early childhood – when there may be an
2149 optimal opportunity to instill long term healthy lifestyles and BMI trajectories.
- 2150 4. Assesses the macro-system level components of community centers and social networks
2151 and the micro-system level components of parent-child genetics on pediatric obesity
2152 prevention

2153 5. Is an easily exportable intervention, and we are actively exploring the opportunity to do so
2154 with the National Association of Counties and the National Recreation and Parks
2155 Association.
2156

2157 **Recruitment**

2158 We will recruit 600 adult parents-preschool child dyads (p/c dyads) to participate in this study for
2159 3-years in duration (**see appendix B for recruitment script**). We will conduct a rolling
2160 recruitment and enrollment strategy for 18-months until a total of 600 parent-child dyads are
2161 enrolled. In order to preserve internal and external validity of the study, the success of any
2162 behavioral intervention is contingent on the researcher's ability to recruit and retain study
2163 participants. Successful retention of this longitudinal study begins at recruitment.

2164 Recruitment efforts consist of a multi-pronged strategy including: site- specific recruitment at
2165 community pediatric clinics, WIC offices, Family Resource Centers and Read to
2166 Succeed/preschool sites, and Coordinated school health sites; study announcements on
2167 English and Spanish radio programs (**see appendix D for invitation letter, language and
2168 scripts will be based from this letter**); and bilingual study recruitment flyers (**see appendix C
2169 for recruitment flyers**) located at neighborhood organizational centers, Walmart, and other
2170 community agencies where families with young children gather (e.g., daycares, pre-K programs,
2171 churches). Due to a highly restrictive eligibility criteria of having a child's BMI needing to be in a
2172 certain range, we will conduct preliminary screens at a location convenient for the family that
2173 could include other community sites (approved by the IRB as a non-research performance site)
2174 or participants' homes, only if requested. In addition to these various approaches, we will also
2175 actively recruit in these other community agencies where families with young children gather. In
2176 addition, we will identify "community liaisons", well-respected persons considered deeply
2177 integrated in the community who have knowledge and relationships to easily reach and
2178 effectively communicate with our target population. Specifically, we will employ 3-6 community
2179 liaisons from each of the two communities (Northeast and South Nashville) to aid in recruitment
2180 and retention activities.

2181 In order to assist in recruiting our hard-to-reach target population, we will also use Facebook as
2182 a viable tool for recruitment. Specifically, we will create a study-specific GROW Facebook page
2183 open to the general public that will serve as an online advertisement. All wording and language
2184 used for this Facebook page-will be similar to our hardcopy flyers that will be disseminated in
2185 the community (**see appendix C for recruitment flyers**). This page will give interested
2186 participants the opportunity to message research staff who can then schedule a follow-up phone
2187 call or meeting. Research staff will also have an opportunity to post status updates on upcoming
2188 recruitment efforts, for example radio announcements or upcoming community-based events
2189 related to the GROW study. Facebook features such as the "like" feature will be enabled
2190 whereby individuals that choose to "like" the GROW study page will be updated via their
2191 newsfeed (the center column of an individual's homepage – a constantly updating list of stories
2192 from people and pages that they follow on Facebook) whenever our Facebook page updates
2193 our status. When individuals "like" this page, it also appears in their respective network's
2194 newsfeeds, thereby potentially exposing the GROW page to other prospective participants.

2195 Participants in the GROW study will also be invited to aid recruitment efforts by voluntarily filling
2196 out the attached referral form at intervention or control sessions with the names, relationship
2197 and contact information of other families they may know with a child age 3 to 5. These referred

2198 families would be contacted and invited to participate in the study by research staff either
2199 by phone or in person. For every family referred who participates in a screening conversation,
2200 the participant would receive a small token gift of appreciation valued at \$5 (e.g., cooking
2201 utensils, key chain, Band-Aid holder, etc.). For every family referred that has met eligibility and
2202 are successfully enrolled in the study, the referring participant would receive a \$10 gift card as a
2203 small token of our appreciation. Word-of-mouth recruitment has been an effective recruitment
2204 strategy in our formative phase work. Including small incentives for participants that successfully
2205 enroll other interested and eligible families, would serve as an additional strategy to assist
2206 recruitment efforts with our hard-to-reach target populations. The maximum number of gift cards
2207 participants will receive for this would not exceed \$100 over the course of the 3-year trial.

2208 From our GROW formative research pilot (IRB No. 100591), out of 439 parent/child dyads
2209 assessed for eligibility, only 50 parent/child dyads were eligible and participated at baseline; a
2210 10% return on investment. Due to the challenge of enrolling in a large, longitudinal, community-
2211 based, prevention trial, another strategy of recruitment will include outreach to patient families
2212 seen by either the Vanderbilt Pediatric Primary Care Clinic or surrounding community practices.
2213 To improve efficiency in light of our restrictive eligibility criteria, we will use Vanderbilt's
2214 StarPanel, a computerized electronic medical record database and Vanderbilt's Whiteboard, a
2215 scheduling database, to generate lists with scheduled clinic dates of potential participants that
2216 meet BMI, age and zip code eligibility criteria.⁹⁴ Specifically, clinic staff will provide a list of
2217 participants to research staff that meet eligibility criteria which serves as a pre-screen to identify
2218 targeted, potentially eligible, participants and invite them into the trial. With these lists, we will
2219 also send out an invitation letter to prospective participants that includes an opportunity to opt-
2220 out recruitment efforts whereby these families that do not wish to be called or approached in
2221 clinic's waiting room, may contact research staff to opt out of receiving any recruitment phone
2222 calls or being approached on-site at clinic (**see appendix D for the invitation letter and D1 for**
2223 **invitation letter in Spanish**).

2224 The Monroe Carell Jr. Children's Hospital at Vanderbilt Division of General Pediatrics serves
2225 families from Davidson County, caring for a panel of 15,000 patients, many of whom reside in
2226 the zip codes of interest (refer to letter of support). Ninety percent of patients qualify for
2227 Medicaid. Moreover, the Cumberland Pediatric Foundation, including more than 200 community
2228 pediatricians in middle Tennessee, will refer eligible parent-child dyads to the study (refer to
2229 letter of support). The majority of children served in these clinics are 5 years old and younger
2230 presenting for well-child examinations. Utilizing this multi-pronged, recruitment strategy, we plan
2231 to reach our required numbers of study participants.

2232 In addition to the recruitment process, the prescreening process has been developed to assess
2233 major elements of eligibility criteria at all recruitment sites (**see appendix E for prescreen**
2234 **survey (English version) and appendix F for prescreen survey (Spanish version)**).
2235 Moreover, recruitment for a few additional sub-cohorts (i.e., ACTIVATE, or GROW Baby), will
2236 include leveraging existing GROW trial participants, whom are eligible and interested. These
2237 cohorts are all designed to minimize participant burden.

2238

2239 ***Informed Consent***

2240 For the GROW trial, informed consent will be obtained on the same day of baseline data
2241 collection. Prior to obtaining the informed consent, adult parents and their preschool-aged child
2242 will conduct a brief eligibility screening, specifically, re-measuring height and weight to confirm

2243 the eligibility requirement of the child's BMI (**see appendix G for script for consenting with**
2244 **children**). If the child participant meets BMI eligibility criteria ($\geq 50\%$ and $<95\%$) then the child
2245 will be escorted to an on-site child activity room, while the parent will be invited to initiate an
2246 informed consent process. In order to minimize participant burden and maximize accuracy, we
2247 may use the child's height and weight prescreening data. Consent for use of this prescreening
2248 data will be obtained by parent as part of the consent process (*see Consent Form*).

2249 Families that do not meet the eligibility criteria will receive a small token of our appreciation of
2250 their time and would not be eligible to participate for the specific cohort recruitment period;
2251 however if they become eligible for future cohort recruitment periods, they could be reassessed.
2252 Participants that do not meet eligibility criteria, data will be destroyed. During prescreen and
2253 prior to baseline data collection, participants have the option to receive information via a variety
2254 of mediums: phone, text or email. Text messages will be implemented by research staff
2255 following phone call contact to remind and confirm upcoming scheduled appointments with our
2256 hard-to-reach target participants, if they so choose.

2257 Informed consent will be obtained in a private space within a public meeting place of the
2258 community center before the initial baseline measurements. While both parents and all in the
2259 family are invited to attend sessions, only one adult (either mother or father) will be present for
2260 the consenting process and enrolled in the program, since the parent or legal guardian must be
2261 willing to commit to the 3-year study (see 11E below for eligibility criteria). During the consenting
2262 process, the child will be escorted to the childcare room located in another room at the
2263 community center.

2264 For all consent forms, we will ask participating adults if they would prefer to use English or
2265 Spanish to understand their role in the research study. With their language of preference,
2266 informed consent forms will be handed to participating adults and then read and reviewed in the
2267 language of preference. We model our current informed consent on our recently completed
2268 study (IRB No. 100591). We include some critical questions to ask parents to ensure they
2269 understand the consent form before signing it. If the participant gives consent, they will sign and
2270 date one copy of the form and keep another for their reference; both forms are also signed and
2271 dated by the study team member obtaining the informed consent.

2272

2273 ***Inclusion Criteria:***

2274 Eligibility inclusion criteria for participation in this study are as follows:

- 2275 • Three-to-five year old children
- 2276 • English- or Spanish-speaking
- 2277 • Child's BMI $\geq 50\%$ and $<95\%$
- 2278 • Parental commitment to participate in a three year study
- 2279 • Consistent phone access
- 2280 • Parent age ≥ 18 years
- 2281 • Parents and children must be healthy (parents with controlled medical conditions will
2282 also be eligible) as evaluated by a pre-screen (**see appendices E & F**)
- 2283 • Child completion of baseline data collection on height and weight, two diet recall
2284 sessions, and at least 4 days of accelerometry and all willing survey items completed by
2285 the parent
- 2286 • Racial and ethnic minority populations disproportionately at-risk for developing obesity

- 2287 • Dyad must be considered underserved which will be indicated by the parents self-
2288 reporting if they or someone in their household participate in one of these programs or
2289 services: TennCare, CoverKids, WIC, Food Stamps (SNAP), Free and Reduced Price
2290 School Lunch and Breakfast, Families First (TANF), and/or subsidized housing.
- 2291 • Residence in or recruitment from one of two Nashville regions: **East Nashville/Region 1**
2292 **(37206, 37207, 37208, 37213, 37216, 37228, 37189, 37115)**: surrounding the East
2293 Community Center and **South Nashville/Region 2 (37013, 37204, 37210, 37211,**
2294 **37217, 37220)**: surrounding the Coleman Recreation Center

2295 For the purposes of this study we define the participating index “parent” as the legal guardian of
2296 the child who identifies that they spend the majority of time with that child at home. Other family
2297 members (e.g., grandmother, uncle/aunt, etc) may be recruited and enrolled in the program only
2298 if they have been granted legal guardianship via court order. During the consent process, legal
2299 documentation will be requested and stored for documentation purposes.

2300 Per COPTR requirement, certain baseline data collection measures must be successfully
2301 completed prior to randomization. Once height and weight, at least two diet recall sessions, and
2302 at least four valid days of accelerometry from the child are completed, and all survey items
2303 families are willing to complete have been collected, parent-child dyads will be grouped into
2304 strata according to parent dominant language preference (English versus Spanish). After these
2305 requirements have been successfully completed, dyads within the strata will then be
2306 randomized to the intervention and control treatment groups.

2307 For the sub-cohort studies, informed consent will be provided at pre-existing data collection
2308 time-points.

2309 For the GROW Baby Sub-Cohort, eligibility criteria are as follows:

- 2310 • Mothers must be enrolled in the GROW Trial, thus meeting its inclusion criteria
- 2311 • Women must report a pregnancy and have a minimum exposure of six hours to the
2312 behavioral intervention or enrolled in the control condition for at least 6 weeks
2313

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2323 For the ACTIVATE Sub-Cohort, eligibility criteria are as follows:

- 2324 • Any GROW parent participant that attend a T5 or T6 data collection time-point.
2325

2326 **Exclusion Criteria**

2327 For the GROW trial:

- 2328 • Children who are <50% BMI or ≥ 95%
- 2329 • Children outside the specified age range
- 2330 • Families who do not speak English or Spanish
- 2331 • Lack telephone contact
- 2332 • Lack parental commitment to participate consistently for a three-year period
- 2333 • Parents and/or children who are diagnosed with medical illnesses where regular exercise might be contraindicated and are not controlled
- 2334 • Children who display dissenting behaviors during baseline data collection
- 2335 • Parents/children who do not otherwise meet the eligibility criteria listed in section above as determined by pre-screen

2338
2339 For the GROW Baby Sub-Cohort, exclusion criteria are as follows

- 2340 • Mothers are pregnant with multiples (i.e., twins, triplets)
- 2341 • Mothers suffer a spontaneous abortion or fetal loss
- 2342 • Mothers are diagnosed as having a high risk pregnancy that cannot be managed conservatively
- 2343 • Infants will be excluded if their estimated gestational age is <36 weeks
- 2344 • Infants have a genetic or medical condition that would significantly alter infant growth (e.g., Trisomy 18)

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2352 Inclusion Statement: **The GROW study operationally defines participants using the**
2353 **following inclusion criteria:**

2354
2355 **GROW Child:** Developmentally normal three-to-five year old children with a BMI ≥ 50% and
2356 <95%.

2357
2358 **Adult:** Healthy adults age 18 or older and designated as the child’s parent or legal guardian.
2359 We will also include adults that have *controlled* medical conditions given that mild-to-moderate
2360 physical activity leads to overall well-being. The informed consent includes information on
2361 potential risks of mild to moderate activity including a statement that encourages participants to
2362 consult their healthcare provider if they are unsure of the safety of engaging in mild-to-moderate
2363 physical activity. All suggested exercises will be mild and are unlikely to cause injury.

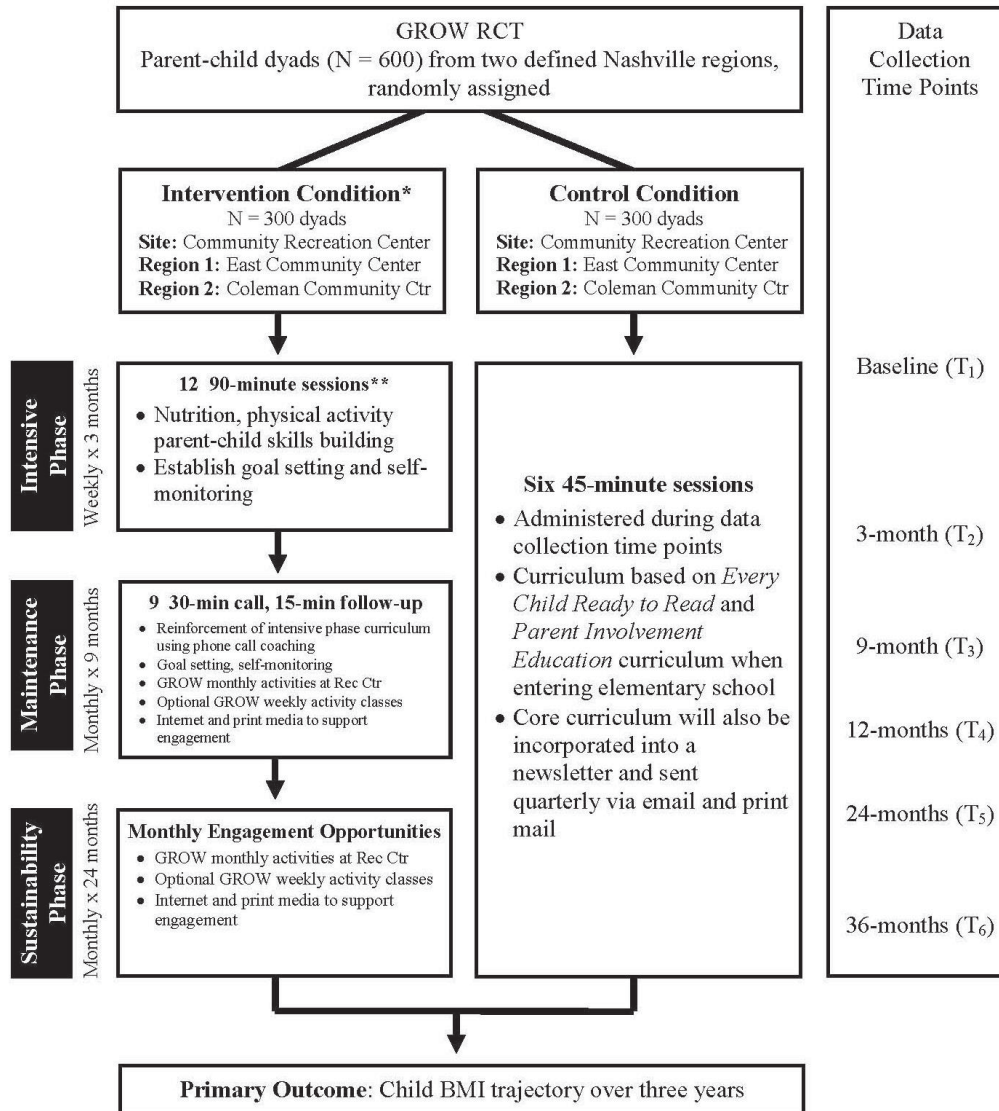
2364
2365 **Family:** Speaks English or Spanish, resides in the defined vicinity of the intervention community
2366 center or control library, has a commitment to the 3-year study, has phone access, and resides
2367 in a household that participates in an assistance program for the underserved (e.g. TennCare,
2368 WIC, SNAP, free/reduced price school lunch).

2369
2370

2371 ***Study Procedural Overview***

2372
2373 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

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

2380 **Study Treatment Groups**

2381 The intervention group will have three phases: 1) an intensive phase (weekly for 3 months) on
2382 nutritional, physical activity and parenting skills-building via 90-min in-person sessions that
2383 promote new social networks (see appendix O for GROW Curriculum and refer to modules
2384 attached). One example of a module would be setting family goals around nutrition and physical
2385 activity. We provide encouragement to utilize the built-environment for routine family physical
2386 activity and access to healthy foods using internet/mail media, email and mail media; 2) a

2387 maintenance phase (monthly for 9 months) via 30-min phone coaching calls to reinforce
2388 concepts from phase one (see appendix I) and a brief 15-min follow-up call one week later (see
2389 appendix J), continued encouragement through internet and mail media, the availability of
2390 weekly activity programming for parent-preschool child dyads through the recreation centers,
2391 and monthly 60-minute GROW events for families to reinforce key messages; and 3) a
2392 sustainability phase (monthly for 24 months), where there is a discontinuation of phone call
2393 coaching and continuation of the other elements from phase two. In addition, for the intensive
2394 phase only, families can select receiving their information via a face-to-face or coaching phone
2395 call sessions (see intervention modules for content and scripts). These phone call sessions will
2396 be 20 minutes in length due to the exclusion of the small group discussion, hands-on activity
2397 with GROW child, and cooking activity, generally included in the face-to-face, in-person
2398 sessions.

2399
2400 The three main pillars of behavior change will be applied at each face-to-face and phone
2401 coaching session: 1) goal setting; 2) self-monitoring to achieve those goals; and 3) problem-
2402 solving. Additionally, after each measurement point in the intervention group, both the parent
2403 and child participants will receive a feedback report on growth in the form of an age and gender-
2404 appropriate BMI curve with an explanation of how their child is growing as well as their own BMI
2405 information with an explanation.

2406
2407 Intervention and control participants will receive a 45-minutes school readiness/school success
2408 program during each of the 7 data collection points. Both conditions will receive a quarterly
2409 school readiness/school success newsletter that will go out via email and snail mail over a
2410 period of 3-years. The core curriculum will be incorporated in the newsletters and will involve
2411 developing parental skills while also creating a practice-based learning environment for parent-
2412 child dyads around school success utilizing key elements of Every Child Ready to Read,⁹⁵ a
2413 project of the Association for Library Service to Children and the Public Library Association (see
2414 appendix P for the Control Curriculum. As children age in the study and enter elementary
2415 school, the control parent-child dyad will receive a curriculum that integrates core elements from
2416 the Parent Involvement Education curriculum, tested and implemented by the Parent Institute
2417 for Quality Education (PIQE) to improve school success.⁹⁶ During the beginning of the study, 1-
2418 2 field trips will be held to expose families to local public library facilities, encouraging their use
2419 of library resources, and introducing them to library staff. In addition to the quarterly
2420 newsletters, control family participants will be receive a calendar of monthly library events (via
2421 email and snail-mail) in order to continuously engage families to resources that integrate the
2422 core curriculum into their built-environment at the public libraries.

2423
2424 Similar to the prescreening process and for the convenience of our study participants, text
2425 messages will be implemented by research staff to remind them of upcoming sessions and
2426 provide them with information relevant to the study aims (i.e., promoting family-based healthy
2427 lifestyles and/or school readiness/school success). If participants would prefer not to be
2428 contacted via text (i.e., text message costs, unreliability, privacy concerns, etc), then we would
2429 refrain from doing so and identify other appropriate means to contact them based on their
2430 preference (i.e., phone calls, newsletters, face-to-face, etc). See Recruitment Eligibility Form for
2431 questions on best way to contact families.

2432
2433 Data collection sessions will be conducted for both treatment groups at 6-points in time (T1-T6):
2434 baseline, 3-months, 9-months, 12-months, 24-months, 36-months, and one at 48-months. Each
2435 of the six data collection points in this study will be conducted on-site at either community
2436 recreational center (i.e., Coleman and East Park) with Metro Parks staff and research staff.
2437 Metro Parks staff will not be "engaged" with research but will handle flow, childcare and check-

2438 in with participants. This data collection process will involve adult-child dyads to proceed
2439 through a variety of stations to gather measurements and information for study analysis. In
2440 addition, make-up data collections sessions will be available for families in all data collection
2441 points. These will occur at a location convenient for the family that could include other
2442 community sites, approved by the IRB for recruitment, and/or participants' homes. Additional
2443 data collections collected yearly will be optional for existing participants (T7 & T8). Like before,
2444 we will obtain consent prior to collecting data at these additional data collection sessions. In
2445 addition, we will request permission to link child health data to school-related outcomes (i.e.,
2446 attendance and test scores).

2447

2448 *Social media use throughout the study for the Intervention Group*

2449 Since our targeted population are underserved families, such families have been well-known in
2450 the literature to be hard-to reach and hard-to-keep families, especially over a 3 year period of
2451 time. Because of this challenge, Facebook has been considered a viable tool to retain and
2452 reach families, in addition, serve as an interactive tool to continually maintain engagement for
2453 participants in the GROW study (see appendix H for Facebook messages). Thus, all study
2454 participants in the intervention groups will be invited to use a social media platform (grow-
2455 program.com). Specifically, participants will receive reminders to upcoming sessions/community
2456 events, polls to gauge satisfaction and curriculum understanding, posts that display recipes,
2457 pictures, and videos, and links to helpful web links for more information. In addition, participants
2458 will be able to post comments and pictures, and potentially strengthen their social network ties
2459 amongst themselves. Per Vanderbilt Social Media Policies, research staff will monitor content
2460 daily to ensure appropriate discourse and interaction that uphold the standards of Vanderbilt as
2461 an institution. For those families that do not have access to this tool, emails and/or regular mail
2462 will be sent out monthly. See attached for our re-engagement letters (in both English and
2463 Spanish) that will be sent to families that have been lost in the study. An additional letter (back-
2464 up) is sent out if there remains no response from these study participants.

2465

2466 *The Adaptive Intervention Design*

2467 The research team plans to utilize an adaptive intervention approach⁹⁷ for children who are not
2468 responding to the intervention based on their BMI trajectories. More simply, for the purposes of
2469 this adaptive intervention, a child will be considered a non-responder if her/his BMI weight
2470 categorization shifts negatively from T1 to T2 (i.e., if formerly normal weight child shifts to
2471 overweight or obese in this period of time; or if formerly overweight child shifts to obese, as
2472 defined by BMI). Child BMI change from T1 to T2 will be reported using an easily
2473 understandable and comprehensive growth feedback report and mailed to the parents after T2
2474 measurements are collected. The adaptive intervention will occur at the first phone call coaching
2475 session of the maintenance phase. The coach will review the feedback report with the parent
2476 and solicit from the parent both the successes and barriers faced with incorporating GROW
2477 lessons into their everyday lives (responders will also receive feedback reports but will not
2478 receive a report explanation session discussed by a phone call coach). These adaptive
2479 intervention report feedback sessions will occur again after BMI categorization/non-responder
2480 status is reassessed at the T3, T4, and T5 data collection time points.

2481

2482 *The Pregnancy Sub-Cohort (GROW Baby)*

2483 The research team will develop a prospective cohort of women who become pregnant during
2484 this ongoing GROW behavioral intervention, designed to prevent childhood obesity in minority
2485 and underserved families. During the trial, if any mother reports a pregnancy, we will invite them
2486 to participate in this new cohort. In order to determine how maternal prepregnancy BMI,
2487 maternal gestational weight gain, and early infant feeding practices interact to shape infant
2488 growth trajectory in the first six months of life, this research team will obtain 1) data on feeding

2489 practices between 3-4 months of child's life via a phone call survey; and 2) data from chart
2490 reviews (OB records and pediatric records), using previously validated abstraction forms for
2491 both pregnancy characteristics and infant growth. The phone call survey has 24 items and will
2492 take approximately 10-15 minutes to complete. Medical records will be obtained from OB/GYN
2493 offices, pediatrician offices, and hospital delivery records. Mothers will sign a release of medical
2494 information for relevant charts, which will be facilitated through the Vanderbilt Clinical Trials
2495 Center. These data will be compared to other baseline demographics, maternal co-variables of
2496 interest and pre-pregnancy anthropometrics (see Pregnancy Cohort Data below for details on
2497 data sources). The development of this type of cohort will provide an opportunity to combine
2498 research-quality anthropometrics and co-variables, already being prospectively collected with
2499 additional patient-reported outcomes and anthropometric measurements, in a natural
2500 experiment to address important questions about pregnancy health and pediatric obesity
2501 prevention in the early stages of life.

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2540 *The Social Network (ACTIVATE) Sub-Cohort*

2541 During T5 and T6 data collection, the GROW Trial has already been approved by Vanderbilt's
2542 IRB to administer the Social Network Survey (see appendix L) that will ask participants to name
2543 up to seven GROW study participants that they consider friends (friendship network). Since all
2544 participants will be asked the same questions, a mapping of the social network will emerge in
2545 the data. From these data we will also be able to weight ties according to strength of friendship
2546 or frequency of communication. Subsequently, in addition to the Social Network Survey, all
2547 families that attend T5 and T6 data collection will be invited to participate in an additional survey
2548 entitled the Patient Activation Measure (PAM), see measures section below for more details.
2549 The PAM survey, a previously validated measure,⁹⁸ is designed to elicit individual's knowledge,
2550 attitudes, skills and confidence in self-managing health. Higher PAM scores suggest that
2551 individuals are more likely to understand that their active involvement is critical to their health.
2552 Data from both surveys will help determine if obesity-related behaviors (i.e., physical activity,
2553 willingness to actively manage one's own health, weight loss) can spread through new social
2554 relationships. Prior to administering the PAM survey, informed consent will be obtained for all
2555 interested participants (see attached consent form lead by Dr. Sabina Gesell from Wake
2556 Forest). Families that agree to consent will then be enrolled in this ACTIVATE sub-cohort.

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2568 ***Outcome Measures & Procedures***

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2571 In addition to BMI as the primary outcome variable, we have seven *a priori* secondary outcome
2572 variables, which were specified after the study began, but before the non-baseline data were unblinded
2573 by arm. Four are related to diet: average daily energy intake (kcal), percentage of energy intake from
2574 fat, carbohydrates, and protein. Two are related to physical activity: average daily time (minutes) spent
2575 in rest and sedentary behavior, and moderate and vigorous physical activity. The seventh variable is
2576 parent community center use with child (never versus at least once).

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2579 ***Process Measures***

2580 The GROW trial process measures will include: participation rates collected via attendance logs;
2581 data collection process collected via timed logs and identification of any issues that arise during
2582 the data collection procedures; retention barriers and facilitators via call logs conducted by the

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2591 study team; session fidelity checks to ensure consistency and accuracy of content
 2592 administration; logs to assess use of recreation center and library outside of mandatory GROW-
 2593 related sessions; Metro Parks and Recreation facility staff satisfaction surveys to assess
 2594 barriers and facilitators of conducting the research program within their facility; library facility
 2595 staff satisfaction surveys to assess barriers and facilitators of conducting the research program
 2596 within their facility; and parent-child satisfaction with study participation. The GROW Trial will
 2597 also administer a brief survey to intervention participants to identify participants' preferences on
 2598 the types of programming delivered by community recreational centers to encourage and
 2599 sustain use of their built environment for physical activity (See Appendix S for survey).
 2600

2601 *Collection of Moderators & Mediators*

2602 Conceptually, moderators identify on whom and under what circumstances the study treatment
 2603 have different effects. In contrast, mediators identify why and how the treatment works or
 2604 doesn't work. Below is a table including all moderators and mediators identified for this study,
 2605 the measurement tool, a brief description, the intended respondent, method and time point of
 2606 data collection. **See Table 1: Collection of Moderators & Mediators below for details.**

2607 Note: Computerized surveys are electronic surveys from the REDCap Database that will be
 2608 administered and completed at the community center; no procedures will be conducted at
 2609 Vanderbilt nor at home. Once entered and saved, the data will be housed on a Vanderbilt
 2610 server. REDCap provides the ability to enter measurement data, including basic mathematic
 2611 and logic checks for verifying valid data, as well as survey data. The research staff will utilize a
 2612 combination of the wireless internet at the community center and mobile hotspots to provide
 2613 internet access for all computers used.

2614 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)	Total calories and macronutrient content (% fat, protein, carbohydrate) adherent to USDA recommendations	P	3-day child diet recall (parental report for child)	T ₁ , T ₄ , T ₅ , T ₆	Yes
	Survey Item					No
	GROW developed survey questions related to intervention messages	Parent and child eating and feeding habits	P	Computerized Survey (9Q)	T ₁ , T ₂ , T ₄ , T ₅ , T ₆	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)	T _{Week 3} , T _{Week 6} , T ₂	Yes
	GROW developed Advice Scale	Assessing information sharing	P	Computerized Survey (2Q)	T _{Week 3} , T _{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.

2616 **Description of Measures**

2617

2618 **Anthropometric Measurements**

2619 Body weight for each subject will be measured, after voiding and wearing light clothing, to the
2620 nearest 100 g on a calibrated digital scale. Body height without shoes will be measured to the
2621 nearest 0.1 cm with a stadiometer. BMI will be calculated (weight [kg]/height [m²]), using the
2622 standard CDC calculator. Both height and weight measures will be collected twice. The mean of
2623 the two closest measures is used as a final measurement. Children will be wearing light clothes
2624 and without shoes. Height without shoes will be measured to the nearest 0.1 cm using our
2625 standard stadiometer (Perspective Enterprises, Portage, MI). Adult and child waist
2626 circumference will be measured with a fiberglass measuring tape on the skin, at the umbilicus,
2627 to the nearest 0.1 cm, according to the recommendations of the World Heart Federation.⁹⁹ Waist
2628 circumference will be collected two times, if the two measurements of waist differ by 1 cm or
2629 more, then the waist measurements are repeated a third time and data entered. The mean of
2630 the two closest measures is used as a final measurement. Measurements will be obtained by
2631 trained project staff and standardized according to accepted standards.¹⁰⁰⁻¹⁰²

2632

2633 **Triceps Skinfolts**

2634 Triceps skinfold thickness is a measure of subcutaneous fat and is a component of equations
2635 used to predict body fat composition.¹⁰³ SFs have been used successfully in studies with adults
2636 and children,¹⁰⁴⁻¹⁰⁶ including young children from 3 to 8 years of age.^{107,108} Recent literature
2637 suggests that SFs are more accurate in estimating body composition compared to bioelectrical
2638 impedance (BIA) during the adiposity rebound, the normal pattern of growth that occurs in all
2639 children growing between 3 to 5 years of age.¹⁰⁷ SF is measured using a Lange skinfold caliper
2640 in the midline of the posterior aspect (back) of the arm, over the triceps muscle, at a point
2641 midway between the lateral project of the acromion process of the scapula (shoulder blade) and
2642 the inferior margin (bottom) of the olecranon process of the ulna (elbow). They are measured to
2643 the nearest 0.1 mm and collected two times. A third SF measurement is taken if either of the
2644 following occur: 1) If the two triceps values are less than 10mm but differ by 2 mm or more; or 2)
2645 If the skinfold is 10mm or larger, with a difference between the two measurements of greater
2646 than 10% (((maximum-minimum)/minimum)*100). In either case, the mean of the two closest
2647 measures is used as the final measurement. In order to accommodate participants that are
2648 morbidly obese participants then we will use the Harpenden calipers. Training, certification and
2649 quality control procedures for SFs are similar to those outlined above for waist circumference
2650 and other anthropometrics.

2651

2652 **Accelerometers**

2653 Amount of physical activity will be assessed using the ActiGraph GT3M (Actigraph LLC, Ford
2654 Walton, FL) accelerometer. Accelerometry had been used successfully in studies with adults
2655 and children¹⁰⁹⁻¹¹³ with a reliability: $r = 0.93$ ¹¹⁴. Both a parent and a child will be asked to wear
2656 the monitor for one week during waking and sleeping hours except when bathing, showering, or
2657 swimming. A simple 1-page manual (in Spanish and English) will be provided. The monitor will
2658 be attached to a belt secured at the waist. The monitors will be sent by mail in pre-addressed
2659 and pre-stamped boxes to the Energy Balance Laboratory at Vanderbilt. We have used this
2660 technique very successfully in similar studies with children and their families. The activity data
2661 will be downloaded to a computer and analyzed. Physical activity will be expressed as activity

2662 counts per day. Total and physical activity energy expenditure (kcal/day) will be calculated using
2663 validated equations.^{114,115} Threshold values from a validation study will be used to calculate time
2664 spent in sedentary, light, moderate, and vigorous activity. Accelerometer use will be
2665 supplemented with a short physical activity log that collects physical activities and time of
2666 accelerometer use (hours/day).
2667

2668 **Energy Intake**

2669 We will obtain detailed data on foods and nutrients associated with energy balance and weight
2670 management from total dietary intakes (foods, beverages and snacks): energy intakes, energy
2671 density, macronutrient intakes, added sugars, as well as consumption of specific foods and food
2672 groups that are excessively high (Sugary Sweetened Beverages, desserts) or inadequate (fruits,
2673 vegetables, milk and dairy products, whole grains and fiber) in the typical diets of U.S. children.
2674 It is understood that accurate assessment of dietary intakes of free-living individuals is a
2675 challenging process and there is no single method that is without limitations. To optimize the
2676 accuracy of the assessment of dietary intake data, we will conduct 24-hour dietary recalls using
2677 the USDA multi-pass method administered by trained diet recall technicians. Recalls will be
2678 performed to capture the average of dietary intakes from 2 nonconsecutive week days and 1
2679 weekend day during the 14-day period of each main study time-point. Diet recall will occur via
2680 three phone sessions conducted by the two master trainers at the University of North Carolina
2681 (UNC) at Chapel Hill over a maximum of a 30-day period to collect complete participant
2682 information. All master trainers will participate in a central in-person training organized by the
2683 Research Coordinating Unit (RCU) located at UNC. No diet recalls will be conducted until after
2684 the trainer has been trained and certified. Parents will report on themselves and on their child.
2685 Analyses will not include data that indicates unrealistically low (eg, <600kcal/d) or high intakes
2686 (eg, >4000kcal/d). Dietary data will be entered and analyzed using our NDS-R software
2687 (Nutrient Data System for Research, St. Paul, MN). Added sugars will be calculated using the
2688 USDA database <http://www.ars.usda.gov/Services/docs.htm?docid=12107>z

2689

2690 **Study Questionnaire**

2691 The study questionnaire will measure a variety of domains and will be provided in both English
2692 and Spanish (**see appendix K for survey**). It will be a computer-administered questionnaire
2693 completed by parents with paper and pencil questionnaire as back-up. **See Table 1: Collection**
2694 **of Moderators & Mediators for details**. Survey takes about 30-45 minutes to complete.

2695 **Metro Parks Staff Questionnaire on Preschool Programs**

2696 This survey will assess programs that promote healthy lifestyle activities for both English and
2697 Spanish speaking families with preschool age children (3-5 years) in the 22 Nashville
2698 Metropolitan Community Recreation Centers. Healthy lifestyle programming includes programs
2699 or events that encourage good nutrition and/or physical activity. In addition to healthy program
2700 availability, this survey will assess the presence of teaching kitchens in each facility, whereby
2701 instructors lead sessions to teach families how to prepare healthy and affordable meals.
2702 Participants for this survey are the 22 facility coordinators at each recreation center. The survey
2703 will be administered annually online through email via REDCap and is expected to take 10-15
2704 minutes to complete. Since all 22 facility coordinator's (directors) emails are publicly available,
2705 we will actively recruit these metro parks staff via email and include a script consenting for their
2706 participation to this online survey (**see appendix R for script**). Results of this survey aim to

2707 describe the presence and frequency over time of healthy lifestyle programs specifically
2708 dedicated to parents and their children at each community center (*see appendix Q*). A waiver
2709 of consent documentation form (Form #1112) has been completed for the Metro Parks staff who
2710 will be consented only before they complete the survey.

2711 **Social Networks**

2712 We will collect social network data, exploring the potential development of new social ties that
2713 could result due to the structure of the study (*see appendix L*).
2714

2715 **Patient Activation Survey**

2716 The Patient Activation Measure (PAM) Survey will also be used to determine if obesity-related
2717 behaviors (i.e., physical activity, willingness to actively manage one's own health, weight loss)
2718 can spread through new social relationships (see attached for survey). The Patient Activation
2719 Measure (PAM) is a 13-item measure that assesses patient knowledge, skill, and confidence for
2720 self-management.⁹⁸ The measure was developed using the Rasch analyses and is an interval
2721 level, unidimensional, Guttman-like measure. Reliability and validity was assessed by Hibbard
2722 et al., with the 13-item measure. Psychometric properties included scores from 38.6 to 53.0.⁹⁸
2723 This survey takes about 5-10 minutes to complete and will be administered at T5, and T6 data
2724 collection sessions. Prior to administering this survey, an additional informed consent form will
2725 be obtained.

2726 **Genetics/Epigenetics**

2727 Saliva will be collected from the parent-child dyad participating in the study¹¹⁶. For adults, saliva
2728 will be obtained utilizing the Oragene saliva kit, collecting 2-3 cc of saliva per participant. For
2729 young children, saliva will be obtained utilizing the "baby brush" approach, in which small
2730 sponges attached to plastic handles are inserted between cheek and gumline to absorb saliva.
2731 Subsequently, the sponges (x4) are cut and placed in the spittoon with DNA preservation
2732 solution. We will then use a modification of the Puregene DNA (Gentra, Inc) Purification
2733 Protocol for 4 ml Saliva Samples¹¹⁶, consisting of 4 stages: (1) cell lysis and addition of RNase
2734 to remove RNA from the salivary nucleic acid; (2) DNA precipitation in 100% isopropanol, with
2735 70% ethanol wash; (3) DNA hydration in reduced TE (Tris EDTA) to approximate concentration
2736 of 200 ng/u; (4) DNA storage at 4C for working stock, and -80C for archival DNA samples.
2737

2738 **Pregnancy Sub-Cohort (GROW Baby)**

2739 These data will be collected in two forms: 1) a phone survey; and 2) data from chart reviews,
2740 using previously validated abstraction forms for both pregnancy characteristics and infant
2741 growth. The phone survey will include questions related to maternal feeding practices between
2742 the child's third and fourth month of life. We will use the Vanderbilt Survey Research Core to
2743 administer the survey via phone. The survey will consist of 24 items and will assess both
2744 parental beliefs and practices about feeding in the first six months of life (see survey attached).
2745 The survey will be administered when the child is between 3-4 months of age to identify feeding
2746 practices when rapid weight gain can be most detrimental and to minimize recall bias. Because
2747 it is a mediator and not a primary outcome, we will only conduct the survey at one point in time
2748 to minimize participant burden. This phone survey will take approximately 10-15 minutes to
2749 complete.

2750 To obtain chart reviews and records, research staff will request medical records via secure fax
2751 from prenatal care, hospital delivery, and nursery records. All chart abstractors will be blinded to
2752 study condition (i.e., intervention or control group). A chart abstraction methodology has
2753 previously been developed to calculate maternal gestational weight gain. We will abstract data
2754 from obstetrical records to obtain at least three additional pregnancy weights, allowing us to use
2755 a slope-as-outcome approach, maximizing our power to detect a clinically meaningful
2756 difference. Specifically, we will obtain information on height, weight, any medical conditions, and
2757 medications they may have taken while pregnant, all of which are typically available in their
2758 existing medical record. To evaluate rapid infant weight gain, we will obtain medical records
2759 from the hospital delivery records for birth weight and from pediatricians' offices for height and
2760 weight measurements through the infants first six months of life.

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2766 **Family Functioning**

2767 Family functioning will be assessed by collecting both: 1) the Family Adaptability and Cohesion
2768 Evaluation Scale (FACES IV), and 2) household social network relationships. The FACES IV is
2769 a 62 item scale that assesses family cohesion and flexibility dimensions, family satisfaction and
2770 family communication styles. There is significant support for the reliability and validity of the
2771 scale and it has been used to assess family functioning in almost 500 published studies.
2772 Coefficient alphas for all scales range from .77 to .89, with the cohesion and flexibility scales
2773 being .89 and .84.^{61,117,118} The two balanced scales, cohesion (7 items) and flexibility (7 items)
2774 assess the emotional bonding between family members and the quality and expression of family
2775 roles and organization, respectively.⁶¹ The additional 4 unbalanced scales assess high and low
2776 extremes of family cohesion (disengaged and enmeshment) and flexibility (rigid and chaotic).
2777 Respondents are asked to respond to each question on a 5- point Likert scale ranging from (1)
2778 strongly disagree to (5) strongly agree. The FACES IV scale has been translated into Spanish
2779 and found to be reliable and valid in Spanish speaking populations.¹¹⁹ The FACES IV will be
2780 completed by all consenting household members.

2781

2782 **Household Social Network Relationships**

2783 Social ties between the GROW parent-child pair, and other participating household family
2784 members will be operationalized as multiple relationships (e.g. familial, friendship, cohabitation).
2785 Size and composition of family network will be assessed. The strength of the relationship ties
2786 will be determined through the FACES IV scales described above. Family Environmental
2787 Factors are collected via survey that is delivered in the parent's language of choice verbally (to
2788 account for low literacy populations) and directly entered a REDCap survey data base.
2789 Additional data that will be utilized to characterize family environment and are already collected
2790 as part of the GROW trial.

2791

2792 **Qualitative Semi-Structured Interviews**

2793 At the study's final data collection, we will conduct a 30-45 minutes semi-structured interview
2794 with GROW intervention families to identify how specific behavioral intervention strategies led to

2795 changes in family environment and young siblings' health behaviors (see attached). Our initial
2796 sample will include 50 families. Should we fail to reach theme saturation with this sample, we
2797 will conduct additional interviews until no new themes emerge. Research assistants will be
2798 trained to code on the three initial transcripts, and certified to work once they meet criteria for
2799 reliable and valid use of the coding system. Twenty-five percent of the transcripts will be coded
2800 twice, with coders kept blind to which transcripts are being used to assess reliability. Coding
2801 discrepancies will be reviewed by the coding team, and feedback used to improve the use of the
2802 coding system. Interviews conducted in Spanish will be translated and transcribed into English.
2803 Interviewers will also collect field notes during the interviews.

2804

2805 Barriers to Physical Activity Questionnaire

2806 This study survey is based from the *Environmental Supports for Physical Activity*
2807 *Questionnaire*¹²⁰ to assess individual perceptions of physical activity supports in the social and
2808 physical environment, use of the built environment, current physical activity behavior and
2809 recreation center use. This survey will take about 15-20 minutes to complete and has been
2810 validated in previous literature.¹²¹ These data will help describe the policy environment of study
2811 participants and identify policies that enable or constrain active living for participants. The
2812 objective of this survey is to link current behavior with local community policies. Specifically, to
2813 determine specific neighborhood characteristics that enable or constrain participant ability to be
2814 physically active, match participant responses to one of the three policy types: personal safety,
2815 transportation, and land use, describe local and state policies that address participant
2816 responses, and identify untapped policy options for improving physical activity levels in
2817 participant communities. **Geographical Information Systems (GIS):** Using data obtained from
2818 external public sources, e.g. data from the Metropolitan Planning Department, the research
2819 team will track and map six key measures of active living over the course of the study, such as
2820 the ratio of sidewalks to road mileage. These data will be compared to the subjective survey
2821 data (i.e., Barriers to Physical Activity Questionnaire – see above) obtained from
2822 participants. GIS spatial analysis will use participant addresses to determine correlations
2823 between proximity to specific features of the built environment (i.e., data from Metro Planning
2824 Dept) and participant data of their perceived built environment (i.e., Barriers to Physical Activity
2825 Questionnaire). In addition, these data will also be correlated with local policies (i.e., external
2826 data) that support activity living and recreational use and tracked over the duration of the study.

2827 A research team member will conduct an environmental audit of those geo-coded regions from
2828 where most of the study participants derive. This will include: 1) block audits where a study
2829 team member verifies the existence of built environment elements such as grocery stores, fast
2830 food establishments, and corner stores; and 2) utilization of the Nutrition Environment Measures
2831 Survey in Stores (NEM-S) to assess the availability and affordability of food/drink in food stores.
2832 Similar to tracking key measures of active living, GIS spatial analysis will use participant
2833 addresses to determine correlations between proximity to specific features of the food built
2834 environment (i.e., environmental audit) and participant data of their perceived food built
2835 environment (i.e., NEM-S). In addition, these data will be correlated with local policies that
2836 support healthy availability and affordability of food, and tracked over the duration of the study.

2837

2838 Control Measures

2839 The study will use Stephanie Carlson's Executive Function Scale for Preschoolers to determine
2840 a comprehensive measure of executive functioning in the child participants of the study. The

2841 battery of hands-on tasks (e.g. card sorting) will be administered by a trained data collector one-
2842 on-one to each child and is estimated to take approximately 10 minutes. To measure
2843 intelligence of the child participants, the research team will use the Woodcock-Johnson III Tests
2844 of Cognitive Abilities – Brief Battery. This tool involves a battery of tasks where children
2845 expressively (verbally and/or through pointing) respond to an assortment of pictures and words
2846 in a flipbook. Trained data collectors will administer this test individually with each child. The
2847 brief battery is estimated to take between 15 and 20 minutes to administer.
2848

2849

2850

2851 **Incentives**

2852

2853 **Data Collection Incentives**

2854 After each data collection session, participating families will receive gift cards of varying
2855 amounts throughout the duration of the 3-year trial. At times 1, 2, and 4 participants will receive
2856 \$40. At time point 5, participants will receive \$50. Also at baseline data collection, families will
2857 receive a small token of appreciation (value of < \$10). At time point 3, participants will receive
2858 \$15 gift card. On the final data collection time (T6), participants will receive \$100. For those
2859 participants that participate in an additional data collection, one year later (T7), participants will
2860 receive a \$20 gift card. See Table 2 below for more details.

2861

2862 In order to maintain the integrity of the research, Quality Control (QC) measures will be
2863 conducted to ensure the accuracy of data collection. Specifically, research staff will be trained to
2864 incorporate one or more secondary measures (i.e., repeat the anthropometric measurements)
2865 that can be used to verify the quality of information being collected from the participant. For this
2866 trial, QC measures will be collected with random participants at all data collection points.
2867 However, due to the additional time and participant burden of these QC checks, an additional
2868 \$10 gift card will be given to participants (i.e., one per parent and child dyad) to compensate for
2869 their time. All QC checks will be conducted by a certified Master Data Collector. These
2870 additional measures will take approximately 15-20 minutes to complete.

2871

2872 Table 2: Data Collection Incentives

2873

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

2874 *Participant will receive half of the incentive upfront prior to wearing the activity monitor and the other half upon its return and
2875 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
2876 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
2877 community center or we will send it via the US Postal Service.

2878 **Because the 3rd part of the incentive is only given after the wearing of the activity monitor and completing 3 of the recalls, we
2879 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
2880 Postal Service.

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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).

2931 **Health-related Incentives**

2932 In addition to these incentives, all participants from both intervention and control groups in the
2933 study will receive family memberships to their respective community recreational center for one
2934 year, which allow adults to use the weight room for no cost. These family memberships will be
2935 given to all intervention families during the study and all control families at the end of the study.
2936 Moreover, if families use the facility at least once per month, then their family membership will
2937 be extended year by year up to 3-years. This will encourage families to utilize their built
2938 environment for family physical activity.

2939
2940 The value of the parent and child gym membership for one year equates to \$400 at each
2941 community center. Although this may be interpreted as undue inducement for families to
2942 participate in a 3-year RCT study, providing gym membership to participants allows increased
2943 physical activity and healthy living - a direct benefit and positive health advantage to subject
2944 participants and their families as opposed to compensation of monetary or economic gains.
2945 Since increasing physical activity is directly related to the outcome of the study, we
2946 conceptualize offering gym memberships as a bonus and a justified benefit for those that have
2947 participated. Compensation will also be given to families participating in the additional sub-
2948 cohorts for this research study. For the GROW Baby sub-cohort, participating women will
2949 receive a small incentive valued at \$20 as a token of our appreciation.

2950 For the ACTIVATE sub-cohort, each parent participant will receive a gift card valued at \$10 for
2951 completing the PAM and Social Network Survey at each data collection point (a total of 2 data
2952 collection points). For all families participating at our data collection sessions, we will provide a
2953 nutritious snack.

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2959 ***Randomization***

2960
2961 Randomization Schedule

2962 An identical randomization procedure will be followed for each of the three successive cohorts.
2963 Available software (e.g., SAS, Stata) will be used to generate a blocked randomization schedule
2964 per each strata, within both regions, resulting in 4 total schedules (2 language conditions x 2
2965 regions = 4). Block size will be randomly permuted with the software procedure (although no
2966 larger than 10), thereby insuring equal representation at intermittent recruitment points while
2967 minimizing the probability of correctly guessing subsequent condition assignment.

2968
2969 Each schedule will be identified by stratum and loaded into the recruitment database. The
2970 database security settings will be specified so that once loaded no one on the study team will
2971 have write privileges for the schedules, and only the statistician will have read privileges. These
2972 settings will prevent anticipation (except for the statistician) or subversion of the randomization
2973 process by any member of the study team.

2974
2975 Random Assignment

2976 Each potential dyad's contact information, including child age and dominant language use, will
2977 be loaded into the recruitment database upon identification as a potential participant and
2978 assigned a unique study identification number (family id). The recruitment database will follow
2979 each potential dyad from the point of identification through eligibility assessment and enrollment

2980 through disqualification or randomization. The recruitment database will track all eligibility and
2981 enrollment criteria and include a utility that checks still-eligible study candidates for criteria that
2982 must be met prior to randomization. Upon identifying dyads who have met all of these criteria,
2983 recruitment staff will engage a database utility that performs randomization by identifying the
2984 stratum into which each potential dyad should be randomized, and populating the next available
2985 slot in the appropriate randomization schedule with the dyad's family id. The database user will
2986 not be able to see, and will be unlikely to anticipate, the arm assignment (treatment versus
2987 control) for each dyad, especially when multiple dyads within a stratum are randomized at once.
2988 Once the dyad is assigned to an arm, a link is established between family id and arm
2989 assignment (treatment versus control). This link will not be writable by any study staff and will be
2990 viewable by the study statistician in the randomization schedules. Dyad's assignments will be
2991 viewable by all study staff on a case by case basis so that the daily activities of managing
2992 participants, both parents and their children, may be done without hindrance.

2993 Randomization Data Management

2994 The link between family id and arm assignment will be stored in the randomization schedule, to
2995 which only the statistician will have read access. All randomized dyads will remain in the
2996 recruitment database for the duration of the study so that recruitment and enrollment reports
2997 can be generated on demand by all study staff. By viewing a dyad's record, any study staff can
2998 view but not edit the dyad's arm assignment.

2999 All dyads' family ids will be exported into a measurement database along with the fields
3000 necessary to conduct timely data collection and on-demand reporting by any study staff. Arm
3001 assignment will not be exported to the measurement database. As such, it will not be possible
3002 for measurement staff to know a dyad's arm assignment based on the information available in
3003 the measurement database.

3004 In addition, once randomized, the family ids (both treatment and control) will be exported into an
3005 intervention database along with the fields necessary to conduct the treatment and control
3006 procedures and allow on-demand reporting. Arm assignment will not be exported to the
3007 intervention database, although its value is implicitly known. As such, intervention staff (in both
3008 the control and treatment conditions) will know which dyads have been assigned to which arm,
3009 but this knowledge is unavoidable and redundant with knowledge that will be apparent from
3010 contact with the dyads within each arm.

3011 Randomization Data Safety

3012 All databases (recruitment, measurement, etc.), will be stored within a password protected
3013 shared drive within the university computer system. All study staff will have access to the
3014 databases upon submitting the required password. Access to tables within these databases will
3015 be made available as needed to perform job responsibilities and in accordance with COPTR
3016 policies. The randomization schedule will not be stored in the intervention database making it
3017 impossible to access in this manner.

3018

3019 ***Risk/Benefit Analysis***

3020 There are minimal research related risks associated with this study. For this study, suggested
3021 exercises will be mild and are unlikely to cause injury. All suggested dietary changes are
3022 evidence-based and healthy. If any physical injury or illness should occur as a direct result of
3023 participation in this study, VUMC maintains limited research insurance coverage for the usual

3024 and customary medical fees for reasonable and necessary treatment of such injuries or
3025 illnesses. The informed consent document will include this statement and will provide pertinent
3026 contact information.

3027
3028 The risks to subjects of the study are reasonable, given their minimal nature (e.g., suggested
3029 low-moderate physical activity options and healthy dietary changes; learning how to engage
3030 their children in dialogue) and given the safeguards employed, as described above. In contrast,
3031 we expect tangible benefits to accrue to all subjects of the study: intervention
3032 group participants are expected to experience improved healthy lifestyle habits and health
3033 outcomes as a result of participating in the study; control group parents are expected to
3034 experience empowerment in their ability to prepare their child for school and control group
3035 children are expected to be better prepared for school as a result of participating in the
3036 study. Also all participants are expected to experience increased parent-child bonding as a
3037 result of participating in the study. All participants will receive family memberships to their
3038 respective community recreational center, depending on which condition will be during or after
3039 study implementation, which allow adults to use the weight room for no cost.

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3042 ***Data Safety and Monitoring Plan***

3043

3044 General Description

3045 Comprehensive measures will be implemented to maintain subject confidentiality as
3046 appropriate. Study ID number will identify all data collection materials for the study. Only study
3047 team members will have access to master linkup lists that match participant names to these
3048 Study ID numbers. The master link-up list linking names and Study ID numbers will also contain
3049 some basic demographics to be collected for purposes of the study (e.g., gender, maternal
3050 education) and personal health information (weight, height, body composition). All data
3051 collection forms will be housed at VUMC.

3052 All study data will be kept at VUMC securely locked in a storage area for this study. All data will
3053 be obtained specifically for research purposes. The study investigators reviewing the data will
3054 not be provided with any participant identification information. Study data collection forms will be
3055 maintained under lock and key for 10 years following completion of the study. Thereafter, they
3056 will be destroyed. All electronic data files will be stored on a password protected, secure,
3057 encrypted server. Only key study personnel will have access to the password. Ten years after
3058 study completion, electronic copies of all datasets will be destroyed. Individuals will not be
3059 identified in any publications of the study findings.

3060

3061 ***Data Safety and Monitoring Plan***

3062 **Purpose:** The Data and Safety Monitoring Plan is written to ensure the safety of the participants
3063 and to verify the validity and integrity of the data.

3064 **Assessment:** Participants will be assessed for adverse events at the time of enrollment and
3065 when the data is collected at each time-point. The Principal Investigator, co-investigators, study
3066 coordinator, intervention lists and all members of the research staff are responsible for the
3067 assessment and reporting of adverse events. All spontaneous reports by subjects, observations
3068 by clinical research staff, and reports to research staff by family or health care providers will be
3069 investigated. The investigators will assess the relationship of the adverse event as not related,
3070 possibly related or definitely related using standard criteria for clinical trials.

3071 **Possible** (to qualify, the adverse event must meet 2 of the following conditions):

- 3072 1) has a reasonable temporal relationship to the intervention,
3073 2) could not readily have been produced by the subject's clinical state,
3074 3) could not readily have been due to environmental or other interventions,
3075 4) follows a known pattern of response to intervention,
3076 5) disappears or decreases with reduction in cessation of intervention.

3077
3078 **Probable** (to qualify, the adverse event must meet 3 of the following conditions):

- 3079 1) has a reasonable temporal relationship to the intervention,
3080 2) could not readily have been produced by the subject's clinical state,
3081 3) could not readily have been due to environmental or other interventions,
3082 4) follows a known pattern of response to intervention,
3083 5) disappears or decreases with reduction in cessation of intervention.

3084
3085 **Definite** (to qualify, the adverse event must meet at least 4 of the following conditions):

- 3086 1) has a reasonable temporal relationship to the intervention,
3087 2) could not readily have been produced by the subject's clinical state,
3088 3) could not readily have been due to environmental or other interventions,
3089 4) follows a known pattern of response to intervention,
3090 5) disappears or decreases with reduction in cessation of intervention.

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3093 **Policy for Blinding in COPTR**

3094 **January 26, 2012**

3095 **Revised July 24, 2014**

3096

3097 **Introduction**

3098 In all clinical trials, the potential for bias is one of the main concerns. Bias arises from conscious
3099 or subconscious factors, and can occur from the initial design through study conduct, data
3100 management, data analysis and interpretation. A general approach to avoid biases is to keep
3101 the participants and the investigators blinded to the identity of the assigned arms until all data
3102 points are collected. As stated by Friedman, Furberg and DeMets, a fundamental point is that:
3103 *"A clinical trial should, ideally, have a double-blind design in order to avoid potential problems of*
3104 *bias during data collection and assessment. In studies where such a design is impossible, other*
3105 *measures to reduce potential bias are advocated."*

3106 **Guiding principle #1:** All COPTR personnel that are in a position to change the study protocol
3107 or its implementation in study participants, should be blinded to information that may allow them
3108 to do so, from when the study starts until the study ends, with specific exceptions as delineated
3109 in this document.

3110 Clarification of terms:

- 3111 • The "study starts" at a site when the first participant is randomized.
3112 • The "study ends" at a site when the outcomes (primary and secondary) of importance to
3113 the site have been collected on all participants.
3114 • "Interim" information is information that is collected between the study start and the study
3115 end at a given site.

3116

3117 As stated in the "Decision Making Protocol," there are Common and Site-specific elements:

- 3118 • **Common elements** refer to those measures that two or more sites collect, protocols
3119 and manual of procedures related to those measures, and reporting processes.
- 3120 • **Site-specific elements** refer to those measures and operational activities that relate to
3121 only one site.

3122

3123 With respect to study information/data, the following is to clarify terms:

- 3124 • Study data – any information collected on study participants, which includes
 - 3125 ○ Primary and secondary outcome variables
 - 3126 ○ Demographic variables
 - 3127 ○ Mediators and moderators
- 3128 • Outcome variables – primary and secondary outcomes as described in site protocols
- 3129 • Process variables – e.g. training, recruitment, intervention implementation, fidelity,
3130 adherence, retention/attrition

3131

3132 Also, data are available at multiple levels:

- 3133 • Individual subject level, including subject’s family or community
- 3134 • Aggregated by arm, that is, collapsed from individual subject level and combined or
3135 averaged by study arm

3136

3137 **Guiding principle #2:** All COPTR study site personnel (staff and investigators) should be
3138 blinded to study data aggregated by study arm that have the potential to impact the study’s
3139 outcome, or if not possible, measures need to be taken to reduce potential bias. Specific
3140 exceptions are delineated in this document.

3141 Study data ‘that have the potential to impact the study’s outcome include aggregated: arm-level
3142 outcome variables, mediators, moderators (OMM), and process variables. Individual level
3143 outcome variables, mediators, moderators, process, and demographic variables are not blinded.
3144 Arm-level demographic variables are not blinded.

3145 There may be specific process data collected in one or more arms that the Principal Investigator
3146 and study staff want to review aggregated by arm before the end of the study. Those variables
3147 will be declared *a priori* by each site, reviewed by the Design and Analysis Working Group, and
3148 approved by the PI. Those variables will be clearly listed as unblinded variables in the final
3149 study protocol. Should sites wish to examine additional blinded process variables aggregated
3150 by arm, after the study has begun, those requests would also be reviewed by the Design and
3151 Analysis Working group and, if access is approved by the PI and by the DSMB, those variables
3152 will be clearly listed as unblinded variables in an amendment to the study protocol. Subsequent
3153 references in this document to process data will distinguish between blinded and unblinded
3154 process variables.

3155 In clinical trials that require **interim** monitoring, it is an accepted principle that interim OMM and
3156 blinded process data aggregated by arm should be kept confidential, with such data accessible
3157 only to a small number of individuals responsible for its analysis and monitoring. Generally,
3158 blinding to intervention arms should be maintained to the extent possible until the study ends.
3159 In COPTR, study investigators and sponsors are not privy to interim OMM and blinded process
3160 data aggregated by arm, and only the study or independent statisticians/analysts preparing and
3161 presenting the analysis to the DSMB, as well as the DSMB, are unblinded.

3162

3163 The study arms in the 4 trials are, BY DESIGN, not able to be totally blinded. However, some
 3164 blinding can be maintained. Measurement staff should not be informed of the intervention that
 3165 individual participants are receiving, and should have **no role** in the delivery of the intervention.
 3166 Efforts should be made to avoid participant (child/parents) interactions that result in open
 3167 chatting with assessors about the interventions they have received. Measurement staff should
 3168 be trained to end any such communication when initiated by participants.

3169 Study investigators and staff are kept blinded as to the ARM level results until study end. That
 3170 is, they should **never** see or hear OMM and blinded process data aggregated by arms until the
 3171 DSMB allows it. Exceptions to this policy are made only for individuals and circumstances in
 3172 which unblinding is necessary for the preparation of reports to the DSMB. Ancillary studies
 3173 need to adhere to these same principles.

3174

3175 **Table 3. Summary of issues related to maintaining objectivity as applied**
 3176 **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 <i>a priori</i> or by amendment to the protocol as unblinded	YES

3177

3178 **Guiding principle #3:** In COPTR, the RCU will function as the ‘Independent Statistician,’ while
 3179 the individual study center statisticians/analysts will function as the ‘Site Statistician.’

3180

3181 The rationale for keeping investigators and sponsors blinded to interim data is generally
3182 accepted. The possible conflict of interest that could arise for the site statistician or analyst who
3183 performs the analysis of the interim data and presents it to a data monitoring committee has
3184 received little attention. Ellenberg and George (2004) describe some potential conflicts for the
3185 Site Statistician, and approaches that might be taken to minimize them.

3186 Ellenberg & George (2004) argue that a reason for not blinding the Site Statistician is the
3187 assumption that the Site Statistician is someone “with no obvious intellectual conflicts of interest
3188 who, by training and temperament, can be trusted to provide a dispassionate analysis of the
3189 accumulating data.” This objectivity assumption may or may not be true, and there are many
3190 pressures exerted on the Site Statistician that is employed and part of the team at a study site.

3191 Each of the 4 COPTR sites has identified an individual(s) who will serve as the Site Statistician.
3192 The **Site Statistician is the person(s) responsible and accountable** for maintaining the blind
3193 of any site-specific study OMM and blinded process data from all other site study investigators
3194 and staff. It is the responsibility of the site Principal Investigator to ensure that the Site
3195 Statistician understands his/her role and responsibilities. The Site Statistician must have no
3196 communication with others at the site, formally or informally, about trends in OMM and blinded
3197 process data and side effects. They must also safeguard data files, printed output, log files and
3198 any emails or correspondence related to the OMM and blinded process data and side effects
3199 with the RCU and the DSMB. It is their responsibility to take care in destroying printouts and
3200 correspondence – ideally by shredding. It is also their responsibility to make sure that any
3201 discussion and communications of blinded data with the RCU and DSMB are confidential.

3202 The Site Statistician:

- 3203 iv. will be blinded to aggregate comparisons by arm of post-randomization COMMON
3204 OMM data until all endpoint data have been collected at their site unless otherwise
3205 instructed by the DSMB.
- 3206 v. will remain objective when carrying out the activities of conducting the trials –
3207 preparing randomization schemes, randomizing individual subjects, processing of the
3208 data, cleaning and editing the data, preparation of analyses/reports of site-specific
3209 OMM and blinded process data, and transmitting the COMMON OMM data to the
3210 RCU; and
- 3211 vi. is responsible and accountable for maintaining the blind of study site investigators
3212 and staff at their site with respect to OMM and blinded process data aggregated by
3213 arm.
3214

3215 The RCU:

- 3216 v. is the only entity that has personnel that are unblinded to the COMMON OMM data
3217 aggregated by arm during the trial;
- 3218 vi. will prepare analyses/reports to the DSMB of the COMMON OMM data and adverse
3219 events aggregated by arm, as requested by the DSMB;
- 3220 vii. shares responsibility for maintaining the blind of study site investigators and staff;
3221 and
- 3222 viii. is responsible and accountable for maintaining the blind of co-investigators from NIH
3223 and RCU staff who do not need to be unblinded with respect to COMMON OMM
3224 data aggregated by arm in order to complete their duties.
3225

3226 **Responsibilities of the Site Statistician and the RCU**

3227 It is imperative that professional ethical conduct guidelines be followed by the Site Statistician
3228 and the RCU Independent Statisticians at each stage of the study. The Site Statistician
3229 prepares the randomization scheme and thus handles the list (datafile, database table, etc.)
3230 linking study ID to assignment that permits looking at the data aggregated by arm. Thus, this
3231 person(s) must exercise care in protecting the treatment allocation list and ensuring no one –
3232 including him/herself - conducts any analyses of COMMON OMM variables, adverse event or
3233 other follow-up information aggregated by arm. The Site Statistician may prepare descriptive
3234 reports of site-specific data aggregated by study arm if so directed by the DSMB or RCU. All
3235 study data must be protected in secure, password protected files or databases with only the Site
3236 Statistician, their programming staff, and the RCU having access to the data files. Note that
3237 data needed to interact with and track families (e.g., names, ages, contact info, etc), will not be
3238 blinded to interventionists, of course.

3239

3240 The list (datafile, database table, etc.) created by the Site Statistician that contains the subject
3241 ID and the allocation to study arm is protected in a secure and password protected manner with
3242 only the Site Statistician and the RCU having access to the information.

3243 **Blinding of Investigators by Data Type**

3244 All data collected will be categorized *a priori* into one of 7 categories:

- 3245 viii. *Demographic* information, such as age, sex, country of origin, and contact
3246 information is not blinded, either at the individual level or aggregated by arm.
- 3247 ix. *Study arm assignment* is concealed until the time of randomization.
- 3248 x. Post-randomization, all field center or site personnel are blinded to *common OMM*
3249 *data, aggregated by arm*, except as allowed by the DSMB.
- 3250 xi. Post-randomization, all site personnel except the site statisticians/analyst are blinded
3251 to site-specific OMM data, aggregated by arm. The site-specific OMM data,
3252 aggregated by arm, are held strictly confidential by the Site Statistician, programmers
3253 they designate, and the RCU as detailed in this document.
- 3254 xii. *Post-randomization, individual level process data* are viewed by the Principal
3255 Investigators throughout the study and may also be shared with the interventionists,
3256 Project Coordinator or Manager. *Arm-level process data* may be viewed by the
3257 Principal Investigators and shared with the interventionists, Project Coordinator or
3258 Manager, if those variables are first reviewed by the Design and Analysis Working
3259 Group, approved for access by the PI, and listed *a priori* as unblinded variables in
3260 the study protocol or as an amendment to the study protocol.
- 3261 xiii. Post-randomization, blinded process data, aggregated by arm, are held strictly
3262 confidential by the Site Statistician, programmers they designate, and the RCU as
3263 detailed in this document.
- 3264 xiv. *Safety data* are collected for the purpose of insuring participant safety. Guidelines
3265 for viewing these data have been designed by the COPTR Subcommittee on
3266 Recruitment, Retention, Consent, Adverse Events and Safety.

3267

3268

3269

3270 **Blinding of Investigators to Study Data by Study Stage**

- 3271 iv. **All baseline data** from an individual subject are collected prior to allocation to a study
3272 arm. Following all baseline data collection on an individual subject, allocation
3273 information on that subject is made available to site study staff as needed.
3274 Comparative baseline (pre-randomization) data may be viewed by investigators and
3275 study staff in aggregate by arm (e.g., for reporting comparability of groups in a
3276 design and/or baseline manuscripts). The site investigators may analyze and publish
3277 data collected at baseline using the usual policies of subject confidentiality and
3278 protection and guidelines set by the COPTR Subcommittee on Publications,
3279 Presentations and Ancillary Studies.
- 3280 v. **Interim Data (post-randomization)**. All analysis of post-randomization data is required
3281 to have discussion and approval by PPA, D&A, the Steering Committee, and the
3282 DSMB, with the exception of analyses conducted by the RCU for purpose of
3283 completing the DSMB report and pre-approved analyses of process-level data. All
3284 site personnel are blinded to *common OMM data, aggregated by arm*, except as
3285 allowed by the DSMB. All site personnel except the site statisticians/analyst are
3286 blinded to site-specific OMM data, aggregated by arm. The site-specific OMM data,
3287 aggregated by arm, are held strictly confidential by the Site Statistician, programmers
3288 they designate, and the RCU as detailed in this document. *Individual level process*
3289 *data* are viewed by the Principal Investigators throughout the study and may also be
3290 shared with the interventionists, Project Coordinator or Manager. *Arm-level process*
3291 *data* may be viewed by the Principal Investigators and shared with the
3292 interventionists, Project Coordinator or Manager, if those variables are first reviewed
3293 by the Design and Analysis Working Group, approved for access by the PI, and
3294 listed *a priori* as unblinded variables in the study protocol or as an amendment to the
3295 study protocol. Blinded process data, aggregated by arm, are held strictly
3296 confidential by the Site Statistician, programmers they designate, and the RCU as
3297 detailed in this document. **No interim OMM or blinded process data from any arm**
3298 **are available for publication or presentation until the end of the study, unless**
3299 **the plan has been (1) reviewed by the Design and Analysis Working Group and**
3300 **the Publications Subcommittee and (2) approved by the site PI, the Steering**
3301 **Committee, and the DSMB.**
- 3302 vi. **Final data**. *Final data* are held private at each site or at the RCU in the same
3303 manner as the Interim data until the end of the study. The end of the study at each
3304 site is defined as the moment that the last study data point at that site has been
3305 collected and recorded. This includes data from all study index children as well as
3306 data from other individuals and entities at a study site. At the end of the study, all
3307 study data, including data on study arm assignment, can be accessed by study
3308 investigators using the usual policies of subject confidentiality and protection and
3309 guidelines set by the COPTR Subcommittee on Publications, Presentations and
3310 Ancillary Studies.
3311

3312 **Preparation of Study Data Reports for the DSMB**

- 3313 v. Accumulated data will be ‘frozen’ at a specified date for the particular report. A copy
3314 of the ‘frozen raw datafile of COMMON measures’ is sent to the RCU for analysis
3315 along with the protected list of the treatment allocation.
- 3316 vi. After processing, cleaning, editing, creating derived variables, the dated ‘analysis
3317 files’ of COMMON variables (including treatment allocation) and relevant
3318 documentation are sent to the RCU. Site-specific data are not sent to the RCU.

- 3319 vii. For COMMON variables, the Site Statistician conducts analyses for the purposes of
 3320 data cleaning and looking for outliers, unusual trends and distributional anomalies of
 3321 the data from their own site, overall – **not** by study arm. They do not generate
 3322 comparative analyses by study arm. Information generated (not the raw data) may
 3323 be shared with other site investigator/s for the purposes of conducting data cleaning.
 3324 The cleaned COMMON variables data are sent to the RCU, along with means and
 3325 frequencies for all variables. The RCU will prepare means and frequencies for all
 3326 variables and compare them to the site results to confirm accurate transfer of data.
 3327 The RCU will prepare descriptive and quality control tables for presentation to the
 3328 DSMB, both overall and by study arm. No modeling is done by the RCU unless they
 3329 are specifically instructed to do so by the DSMB.
- 3330 viii. For **site-specific** data, the Site Statistician conducts analyses for the purposes of
 3331 data cleaning and looking for outliers, unusual trends and distributional anomalies
 3332 from their own site, in a manner similar to that described above for COMMON
 3333 variables. Different from common variables, the Site Statistician prepares descriptive
 3334 and qualitative data reports using templates developed in cooperation with the RCU.
 3335 These reports will not be generated by study arm unless instructed to do so by the
 3336 DSMB. Otherwise, site-specific variables will be examined only with data from all
 3337 study arms combined.
 3338

3339 **Data on Participant Safety**

3340 As with other data, safety data will be blinded, as possible, to the investigators and staff at each
 3341 site (not possible when obviously related to the intervention or collected during an intervention
 3342 activity, for example). The objectively collected adverse events data, however, are collected the
 3343 same way in all arms and will be blinded. Sites should see only aggregate data (all treatment
 3344 arms combined) although RCU can prepare data for DSMB by arms.

3345 **Treatment condition unblinding recommendations**

3346 Study arms

3347 Decisions to unblind the site investigators to arm-level experimental assignment will be the
 3348 responsibility of the DSMB according to the following steps.

- 3349 vi. RCU prepares adverse events and safety reports by unidentified arm (e.g., group A,
 3350 group B) in the twice-yearly DSMB reports.
- 3351 vii. DSMB reviews adverse events and other safety-relevant data at their periodic
 3352 meetings.
- 3353 viii. If the DSMB identifies a potentially important difference between arms in adverse
 3354 events or other safety-related data, they may request additional analyses and/or
 3355 request unblinding of arm assignment (e.g, treatment and control), and may consult
 3356 with the NIH, RCU and PI(s) to help them interpret the findings. Unblinding, if
 3357 necessary, should be limited to only those investigators who need to know to protect
 3358 the safety of participants.
- 3359 ix. If the DSMB determines that the differential between arms may impact the safety of
 3360 participants and/or changes the assessment of risk of participation, they will make
 3361 the appropriate recommendation to the NIH who, in turn, will notify the site PIs,
 3362 accordingly.
- 3363 x. It is the responsibility of the site PIs to report to their site IRBs.
 3364

3365 **Presentation of Reports to the DSMB**

3366 The RCU statisticians will be presenting the report, which includes the report on the common
3367 measures, plus each site’s site-specific variables report. The Site Statisticians are available to
3368 be contacted by phone during the DSMB meeting in case questions arise that they are in a
3369 better position to answer about the site-specific variables and the overall site analyses. Site
3370 Statisticians may not participate in any portion of the meeting or call in which unblinded common
3371 OMM data are discussed.

3372 **Timeline for preparation of reports to the DSMB**

3373 Typically there is a roughly a 7-week period prior to the date of the meeting for preparing the
3374 DSMB report. Adherence to this timeline assumes that data entry and cleaning have been
3375 ongoing and that templates used to generate tables have already been created. It also
3376 recognizes that some data, such as blood analyses, actigraph, and diet data, that undergo other
3377 processing, may be delayed in comparison to other types of data.

3378 **Table 4. Timeline for preparation of reports to the DSMB**

-7 weeks	<ul style="list-style-type: none">• data ‘frozen’ for the report on same date at each field site• copy of raw frozen COMMON measures files sent to RCU
-5 weeks	<ul style="list-style-type: none">• data processing, data cleaning, data editing, datafile creation at each field site completed• clean COMMON measures files sent to RCU
-3 weeks	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• RCU compiles reports, assembles binders and sends to DSMB
0 weeks	<ul style="list-style-type: none">• DSMB meeting

3379

3380 At the meeting, the RCU presents the report, and afterwards collects all reports for archival. The
3381 RCU communicates with site investigators and Site Statisticians on relevant issues raised by
3382 the DSMB – such communication is not shared with other site staff or investigators.

3383 **Communication of the Policy for Blinding in COPTR**

3384 In order to insure that this policy is clearly understood and communicated, all COPTR study
3385 Principal Investigators, the NIH Project officer, the Site Statistician and the RCU members
3386 involved in data management or analysis will confirm compliance. Over the course of the study
3387 as new personnel are hired, they will also confirm compliance. This will be done by each of
3388 these individuals sending an email to the COPTR Communications Manager as follows:

3389 I have read, understood and agree to comply with the 9 page document entitled,
3390 *Policy for Blinding in COPTR.*

3391 The RCU will maintain a list of the names of individuals from whom this confirmation has been
3392 received, and this list will be available for inspection by the DSMB.

3393

3394

3395 **References**

- 3396 3. Ellenberg SS, George SL (2004) Should statisticians reporting to data monitoring
3397 committees be independent of the trial sponsor and leadership? *Statistics in Medicine*
3398 23:1503–1505.
3399 4. Friedman LM, Furberg CD, DeMets DL (2010) Fundamentals of Clinical Trials, 4th ed.,
3400 Springer, NY.

3401

3402

3403 ***Study Design, Statistical Consideration and Analysis Plan***

3404

3405 Study Design

3406 The design of the study is a longitudinal non-blinded (open) randomized control trial. Within
3407 each of two sites, adult-child dyads with children ages 3-5 years will be randomly assigned,
3408 stratified according to parent language use (English or Spanish), to either the three-year
3409 prevention program or the control condition. Assessments will occur over six time points within
3410 each cohort, beginning at baseline and including assessments post-intervention (at 12 weeks/3
3411 months), and at 9, 12, and 36 months from baseline.

3412

3413 Primary Research Question and Hypothesis

3414 Our primary research question is about the impact of the GROW trial on the growth rate of
3415 children's BMI over time. Specifically, we hypothesize the following:

3416 Hypothesis 1: The BMI trajectories of children in the treatment group will change at a slower
3417 rate than those in the control group over time.

3418

3419 Primary Outcome

3420 Although childhood obesity is a well-documented public health concern, most studies have
3421 assessed the obesity outcome (e.g., BMI) using only a single time point or incorporating a pre-
3422 post design, leaving us with little knowledge about the actual shape or growth rate of trajectories
3423 of BMI during this critical period of development. Indeed, few studies have taken a
3424 developmental perspective in order to understand how and when obesity develops in early
3425 childhood. By measuring BMI at multiple time points, we will examine growth trajectories in early
3426 childhood. This will allow us to examine the effect of a prevention program on these varying
3427 trajectories (Agras, Hammer et al. 2004; Pryor, Tremblay et al. 2011). As Barker et al.
3428 demonstrated, it is the change in BMI over time in early childhood, rather than BMI at any one
3429 time point, that is linked with health consequences in adulthood (Barker, Osmond et al. 2005).
3430 Moreover, an earlier childhood adiposity rebound is associated with an increased risk of later
3431 obesity (Rolland-Cachera, Deheeger et al. 1984; Cole 2004). Because clinical literature about
3432 childhood obesity indicates that the shape of the BMI trajectory across ages three to eight is
3433 curvilinear, we will account for this in our analytic plan (Kuczmarski, Ogden et al. 2002; Cole
3434 2004) (see below).

3435

3436 Primary Analysis

3437 Statistical model and approach

3438 Our primary analysis will be an intent-to-treat analysis, and we will fit a multilevel mixed-effects
3439 linear model using a maximum likelihood procedure to handle missing data.

3440 Time-varying BMI will be the outcome at Level 1 nested within children at Level 2. Time at
3441 Level 1 will be in years since baseline as computed from the date of each child's measurement
3442 at each time point. The following child-level (Level 2), time invariant variables will be predictors
3443 of the linear and quadratic BMI growth rates and the intercept at Level 1: age at baseline
3444 (centered at a value of interest) and random assignment to intervention or control. Child gender
3445 will be a child-level (Level 2), time invariant predictor of the intercept at Level 1. This approach
3446 allows the estimation of growth rates based on each child's individual measurement dates, and
3447 accounts for both age at baseline and time in the study.

3448 The Level 1 equation is as follows:

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

3449 where BMI for each child i is repeated over time t . BMI for a given child is a function of the
3450 individually varying baseline intercept π_{0i} , the linear growth rate π_{1i} across 36 months, the
3451 quadratic growth rate (acceleration) π_{2i} , and a random error term.

3452

3453 The intercept and two growth parameters will then be regressed on Level 2 (child-level)
3454 predictors as follows:

3455 BMI Intercept: $\pi_{0i} = \beta_{00} + \beta_{01}(age - C)_i + \beta_{02}(I)_i + \beta_{03}(F)_i + r_{0i}$

3456 Linear Growth: $\pi_{1i} = \beta_{10} + \beta_{11}(age - C)_i + \beta_{12}(I)_i + r_{1i}$

3457 Quadratic Growth: $\pi_{2i} = \beta_{20} + \beta_{21}(age - C)_i + \beta_{22}(I)_i + r_{2i}$

3458 where I is an indicator for group assignment and equals 1 for the intervention group and 0 for
3459 the control group, and F is an indicator for sex and equals 1 for females and 0 for males. β_{00} is
3460 the mean initial BMI in control group males while adjusting for child age at baseline (centered),
3461 β_{01} is the effect of child age at baseline (centered) on initial BMI, β_{02} is the effect of being
3462 assigned to the intervention group on initial BMI (expected to be 0), β_{03} is the effect of being
3463 female on initial BMI, and r_{0i} is the random error variance. β_{10} represents the linear growth rate
3464 at baseline in the control group while adjusting for child age at baseline, and β_{11} is the effect of
3465 child age at baseline on linear growth. β_{12} is the intervention effect on linear growth, and β_{22} is
3466 the intervention effect on BMI acceleration while adjusting for child age at baseline.

3467 The Level 1 and Level 2 equations can then be combined and regrouped to yield a single
3468 equation for the model:

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

3469 where the terms in the first bracket contribute to the intercept, the second bracket's terms
3470 contribute to the linear growth, the third bracket's terms contribute to the quadratic growth, and

3471 the final bracket contains all of the random error terms. We will specify an unstructured
3472 variance-covariance matrix.

3473 We will conduct a likelihood ratio test with two degrees of freedom to test whether the linear and
3474 quadratic intervention effects (β_{12} and β_{22} , respectively) are jointly equal to zero. If this joint test
3475 is not significant at $p < 0.05$ then intervention effectiveness is not demonstrated. If this joint test
3476 is significant at the $p < 0.05$ level, then the intervention effect was significant.

3477

3478 *Checking and Sensitivity Analyses:* Once a model has been estimated, we will need to
3479 investigate its properties not only to ensure that any data idiosyncrasies do not impact the
3480 results but also to help ensure that the results are generalizable. The first issue is to check for
3481 systematic differences between the model and the data using graphs, such as comparisons of
3482 predicted and observed values of BMI, and other standard diagnostics (Snijders 2008). An
3483 extension of this idea is to simulate new sets of outcomes, based on our model, and use the
3484 simulated data as a reference test group by comparing this set to the observed result; in this
3485 case, we would look for situations in which the data appear different from what we would expect
3486 by using the model to predict the data (Gelman 2007).

3487

3488 A second issue is whether we have left out important features of the model, including, for
3489 example, (1) age at randomization, (2) measurement occasion, (3) study wave (by which we
3490 mean enrolled in first year, second year, or third year of the program), or (4) other demographic
3491 variables (e.g., SES, parent level of education) or substantive covariates (e.g., maternal
3492 depression). Some of these variables will be tested explicitly as moderators or mediators (see
3493 previous sections pertaining to moderators and mediators as well as sections 11.6 and 11.7
3494 below). In addition, trajectories may vary by baseline BMI; this possibility will be checked by
3495 estimating a model with a baseline BMI by treatment group interaction. We will estimate
3496 additional models that include one or more of these additional features to check whether
3497 inclusion of any of these predictors is both statistically reasonable and affects our conclusions.

3498

3499 A third issue is whether age is correctly specified. With six data points, a limit exists as to what
3500 can reasonably be done. We suggest that the quadratic model should be checked in two ways:
3501 (1) substitute linear splines with a break between, for example, ages 4 and 5 (anticipated
3502 adiposity rebound timing); (2) substitute non-linear splines, in particular, restricted cubic splines
3503 with 4 knots chosen following Harrell's default positions (Harrell 2001).

3504

3505 A fourth issue relates to the potential correlation among the clusters/subgroups in our analysis:
3506 to what extent are these clusters correlated, what is the effect of that correlation on our results,
3507 and how accurately have we specified the clusters? Although we will not use the cluster-
3508 adjusted robust sandwich estimator in our primary analysis, we will, as a safeguard, fit a model
3509 that assumes a cluster structure within the data and compare the standard errors of this model
3510 to those from our primary model. If there are substantive changes in the standard errors, further
3511 work will be done to see which set of standard errors is more appropriate in our situation.

3512

3513 Missing data including level of attrition, lost to follow-up, and missing data treatment

3514 Estimated Attrition: Within each planned cohort of 200 dyads per three cohorts, six waves of
3515 data collection will occur, with shorter time intervals between the earlier waves and longer time
3516 intervals later. According to prior community-based studies, subject dropout decelerates over
3517 time, with the worst losses occurring early. We will make every effort to reduce attrition, with
3518 particular focus on the earlier waves of the study, to ensure that we retain at least 80% of our
3519 sample within each cohort, yielding a cohort size of at least 160 and a total sample size, at
3520 study end, of at least 480. This level of attrition would leave us sufficiently powered (.90) to be
3521 able to detect a standardized effect size of .40 (a respectable and common effect size unique to
3522 the analytic method we are using--see sample size and power analysis section). An even larger
3523 sample size will increase the power to detect a meaningful difference, as explicated in the
3524 power analysis and sample size section below, and we will strive to ensure that the sample is as
3525 large as possible at each successive wave. In addition, it is important to note that our analysis is
3526 an intention-to-treat analysis. Accordingly, we will use all cases in our analyses, even those with
3527 as few as one wave of data, such that attrited cases will not truly be lost but instead retained in
3528 our analytic procedures.

3529

3530 Missing Data: Conceptually, we anticipate two types of missing data: (1) people who drop out
3531 after a measurement occasion and never return [i.e., lost to follow up]; and (2) people who miss
3532 one or more particular measurement occasions (e.g., occasion three) but are present for each
3533 of the others, at least one of which is later in time than the one (or more) that they missed.

3534

3535 With six repeated measurements, some participants inevitably will miss one or more occasions
3536 of outcome data collection. One advantage of the mixed models over older repeated measure
3537 ANOVA models is the use of all available data without dropping any subjects (Nich and Carroll
3538 1997). We begin by assuming that the missing occasions meet MCAR or MAR assumptions
3539 (Little and Rubin 2002). If so, the results of the mixed model (e.g., the effect of time, group by
3540 time) are robust.

3541

3542 To guard against missingness biasing results, we will also conduct secondary analyses of
3543 missingness to see how realistic the assumption of MAR or MCAR may be. This check can be
3544 done in several ways. We will start with descriptive statistics comparing the characteristics of
3545 observations with and without missing values (e.g., gender, baseline BMI, age at enrollment,
3546 etc.). The first analysis will use standard multiple-imputation with 100 imputations (Little and
3547 Rubin 2002). Three possible directions, in addition to standard diagnostics (White, Royston et
3548 al. 2011) can be pursued when checking whether being missing is non-random (i.e., in checking
3549 the results of the multiple imputation):

3550

3551 1) The first method is our primary suggestion: we will impute the data using standard
3552 multiple imputation (MI) software but with constraints on the values that can be imputed.
3553 These constraints arise because our prime concern regarding non-random missingness
3554 is that either those who don't need the program (i.e., those who are lean) or those who
3555 perceive that they are not seeing an effect (i.e., who are, and remain, overweight) will
3556 miss occasions. For example, in one set of imputations we would constrain all imputed

3557 BMIs to be below, say, "a"; in a different set, we would constrain the imputed BMIs to be
3558 above, say, "b"; this type of constrained MI is discussed in An and Little(An, Little et al.
3559 2010) and Jenkins, Burkhauser, Feng, and Larrimore(Jenkins, Burkhauser et al. 2011).
3560 One hundred imputations will be used for each such constrained MI. We will examine
3561 the BMI pattern of those who drop out and, if we see evidence of either "a" or "b", use
3562 the values we observe to set the constraints.

3563 2) A second possible type of sensitivity analysis was originally suggested by Rubin (1987)
3564 and has been extended by Carpenter, Kenward, and White,(Carpenter, Kenward et al.
3565 2007) who suggest weighting each imputed result (rather than Rubin's standard simple
3566 averaging of the results), where the weight depends on the assumed departure from the
3567 MAR assumption. Their technique relies on at least one strong assumption, but they
3568 provide a graphical diagnostic to help check this assumption.

3569 3) If drop-outs (situation one above) are much more common than missing an occasion and
3570 then returning (situation two above), we will estimate a pattern-mixture model (Little
3571 1993; Hedeker and Gibbons 1997). If missing one or more occasions and then returning
3572 is relatively common, however, we will not pursue this strategy.

3573

3574 Detectable Difference, Sample Size, and Power

3575 Power and Sample Size Estimation: The power analysis was performed on our primary analysis
3576 (see below): a quadratic model of the BMI trajectories. For our sample size estimation, we used
3577 the OD (Spybrook 2011) software so that we would be consistent with our planned analysis.
3578 This software allowed us to examine two-group repeated-measures trials with quadratic change,
3579 the same model being used for the analysis.

3580

3581 This software uses a standardized effect size as defined in Raudenbush and Liu, namely, the
3582 group difference on the polynomial trend divided by the "population standard deviation of the
3583 polynomial trend of interest" (p. 391; the "population standard deviation" refers to the square
3584 root of the variance of the random effect) (Raudenbush and Xiao-Feng 2001). This specification,
3585 particularly the denominator, is quite different from cross-sectional standardized effect sizes
3586 such as Cohen's D, given that, with a polynomial model (here quadratic), the difference between
3587 groups depends on the point in time examined. In particular, given our hypothesis (see below),
3588 we expect that, after adiposity rebound is reached, the BMI of children in the intervention group
3589 will grow more slowly than that of children in the control group such that the differences between
3590 their mean BMIs will increase over time. Our expectation implies that we are interested in the
3591 significance of the quadratic term in the model, and expect that the difference between the
3592 control and treatment group quadratic effect will be significantly different from zero.

3593

3594 We note one difference between the OD program's assumptions and our study: the OD program
3595 assumes that the measurement occasions will be equally spaced over time, which is not the
3596 case in our study. As a result, specifications from the OD program may lead us to overestimate
3597 power and underestimate sample size. Power is high in the current study, as can be seen in the
3598 table below, thus we expect that these potential mis-estimations are not problematic.

3599

3600 To determine the power and effect size of the current study, we need estimates of the
3601 standardized effect size, which we obtained from a subset of our previous Salud Con La Familia
3602 study. We used only a subset of the Salud subjects because the inclusion criteria for that study
3603 (i.e., children at any level of baseline BMI) were broader than for the current study (i.e., children
3604 whose baseline BMI is between the 50th and 95th ([or 99th] percentile). For our estimations, then,
3605 we used only the Salud data for those from the 50th to the 95th percentile (and then again from
3606 the 50th to the 99th percentile [see below]). Other important differences exist between Salud and
3607 the current study, however, that limit our ability to estimate power and sample size based solely
3608 on Salud: (1) the Salud subjects had only three measurement occasions which covered 15
3609 months rather than six occasions over three years (the GROW trial) and (2) the Salud
3610 intervention was comparable only to the 12-week intensive phase proposed in the GROW study
3611 and did not include a maintenance or sustainability phase as proposed in the GROW trial. We
3612 expect that the increased number of sessions as well as the intensity of the intervention in the
3613 GROW trial will serve only to increase the power of the GROW study.

3614

3615 When using the OD software, the user can set various values, the most important of which is
3616 the standardized effect size discussed above. Other possible values to set include the duration
3617 of the study (here, three years), the number of measurement occasions (here six), and the
3618 variance of the residuals and the variance of the random effects. We found that even fairly
3619 sizable changes in value used for the residuals and the variance of the random effects had little
3620 effect on the projected sample size (e.g., holding other elements constant and changing the
3621 variance of the random effect of age-squared from the observed standard deviation of 2.8
3622 [based on the Salud data] to the OD program's default of 1, only increased the sample size at a
3623 power of 0.8 by about 20 subjects). Using the program defaults for residuals and variance of the
3624 random effects was a conservative (i.e., produced larger estimates of sample size) approach
3625 compared to using the results based on Salud, thus we used these defaults in the table below.
3626 Changing the standardized effect size does have important consequences for the estimated
3627 sample size, however (see Table 5).

3628

3629 As previously stated, we used the Salud data to estimate our primary model (see below) for
3630 those within that study who were between the 50th and 95th BMI percentiles at baseline. The
3631 control group in the Salud data showed unexpected results with virtually no non-linearity (i.e.,
3632 their BMI trajectories increased but in a linear fashion over a 15 month period), therefore we
3633 believe that the effect size from that model, which was quite large and based on different
3634 assumptions, is an overestimate of the effect that we will see in the GROW study. Instead we
3635 used the OD program default for the effect size of 0.4, a commonly used effect size in
3636 longitudinal studies and thus the OD program default, to estimate our required sample size.
3637 Accordingly, Table 5, below, indicates, for powers of 0.7, 0.8, and 0.9, the estimated sample
3638 size using the OD program for the default effect size (0.4) and for two additional effects sizes, a
3639 smaller and more conservative effect size (0.3) and a larger and more liberal effect size (0.5).
3640 As the table below indicates, we estimate that retaining a sample size of at least 480 will leave
3641 us adequately powered to determine this middle/medium effect size of 0.4.

3642

3643 **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 (<i>OD program default</i>)	Sample size for Standardized Effect size = 0.5
70.00%	500	285	186
80.00%	640	360	232
90.00%	860	480	308

3644

3645 Because the results of our pilot study currently underway have led us to consider including
3646 children with higher baseline BMI in the GROW trial than we had originally planned, we also
3647 estimated our primary model on Salud participants who were between the 50th and 99th
3648 percentile of baseline BMI to determine the effects of including these children with a higher BMI.
3649 While, as expected, the variance increased when we moved to the model that added children
3650 between the 95th and 99th percentiles, the difference between groups (control and intervention)
3651 also increased such that the standardized effect size changed very little and, thus, there was
3652 virtually no effect on power (i.e., the desired sample size, under various conditions, never
3653 changed by more than two people). If, then, we decide to extend our criteria in the GROW trial
3654 to include children who are in the 95th to 99th percentile of BMI at baseline, our analyses will
3655 continue to be sufficiently powered.

3656

3657 Currently, the design for the GROW trial includes 600 children, and, though we would expect to
3658 be adequately powered at a smaller number of subjects, we plan to recruit 600 subjects to allow
3659 for potential attrition. We note, however, that if recruitment of that higher number of subjects
3660 becomes problematic (and we have observed in our current pilot study the difficulties inherent in
3661 recruitment for a similar prevention trial), we will stop subject recruitment at a smaller number of
3662 subjects, though ideally not less than 480 (see Table 5), such that we are adequately powered.

3663

3664 Analysis for Possible Effect Modifiers

3665 The variables that are listed in the previous section as moderators (e.g., race/ethnicity, genetic
3666 risk score, etc.) will be entered appropriately into the analytic model as interaction terms in order
3667 to test the effect of the moderator on the outcome (child BMI trajectory). Relevant three-way
3668 interactions (e.g., child gender by age by group) will also be tested.

3669

3670 Analysis for Possible Effect Mediators

3671 The variables that are listed in the previous section as mediators/covariates will be entered into
3672 the analytic model as time-varying covariates and their effects on the outcome will be assessed
3673 accordingly, controlling for all else in the model.

3674

3675 Secondary Hypotheses and Analysis

3676

3677 Secondary Analyses: We list below two sets of secondary analyses. The first is specific to our
3678 primary analysis (see Aim 1, Hypothesis 1); the second is specific to the secondary aims and
3679 related hypotheses (see Aims 2-6) and contained under section 11.9 (below).

3680

3681 **Secondary Analyses in relation to the Primary Hypothesis and Analysis**

3682

3683 1) Timing of adiposity rebound: We anticipate that we will be able to characterize and
3684 capture the timing of adiposity rebound for many of the children enrolled in the study. At
3685 time of enrollment, each child is at least three years of age and is less than six years of
3686 age (and we will know, including fractions, how old they are at enrollment by collecting
3687 their date of birth); measurement occasion six will occur at least three years after
3688 enrollment. Using these conditions, those who enroll on their third birthday will be at
3689 least six years old at measurement occasion six (and everyone else will be older); in this
3690 scenario it is reasonable to assume that most subjects who enroll at age three will have
3691 reached adiposity rebound by measurement occasion six, although we will miss some
3692 children who have earlier/later rebound timing. Also, virtually all children who enroll at
3693 age four should experience adiposity rebound during the study, but a few might be
3694 earlier than four or later than seven. Finally, the majority of those who enroll at age five
3695 should experience adiposity rebound during the study, but a minority will have
3696 rebounded prior to age five. Note that the mean age at adiposity rebound is a simple
3697 function of the coefficients from the main model: $-\beta_2/(2*\beta_3)$ will be the nadir for the control
3698 group (and a similar calculation captures the intervention group:

3699 $-\beta_4/(2*\beta_5)$).

3700 2) The effect of parental change in BMI over the study period on child's growth trajectory: In
3701 this study, this effect will be modeled by including baseline BMI of the parent as a
3702 predictor, and also including other measures of parent BMI as time-varying covariates
3703 (i.e., the value of the covariate depends on the measurement occasion).

3704 3) We will test the difference between mean BMI for both groups at the end of the trial (36
3705 months) to determine whether they are significantly different from one another, thus
3706 adding additional information to our analyses.

3707 4) We will test whether the trajectories of both normal and overweight children in the
3708 treatment group accelerate at a slower rate than those in the control group over time,
3709 such that those in the treatment group will be less likely to evidence trajectories of
3710 obesity compared to those in the control group. Each child will be categorized as having,
3711 or not having, an acceptable BMI trajectory. This binary variable will be the outcome
3712 variable for this secondary analysis. We will test this first, in an unadjusted analysis (a 2
3713 by 2 table where one variable is the outcome variable and the other is group [control or
3714 treatment]), and then in an adjusted analysis using logistic regression. Predictors in the
3715 logistic regression will include demographics (e.g., gender) and various baseline
3716 variables, including the baseline BMI weight category (i.e., normal or overweight).

3717 5) In a series of secondary analyses, we will examine the random-effects in more detail:

- 3718 1. Using our original fitted model, we will impose an independent covariance matrix
3719 (which assumes no correlation between random effects), reducing the resulting
3720 number of random effects from seven to five. The results of this change to the model
3721 will inform us about the next two steps (see below).
- 3722 2. We will add the two age-squared terms (for intervention and control) as random
3723 effects, continuing to use the independence structure, and bringing the number of
3724 random effects back to seven.
- 3725 3. Keeping the two age-squared terms as random effects, we will return to an
3726 unstructured covariance matrix, bringing the number of random-effects to 13.
- 3727 4. At each step in the above process, we will evaluate the results of continuing to add
3728 additional random effects terms, including noting model convergence problems.
3729 While we believe the model with 13 random effects will have reduced power and thus
3730 do not propose this model for our primary analysis, we believe that fitting this model
3731 in a secondary analysis, via the systematic steps outlined above, will allow us to
3732 examine the consequences of including a large number of random effects and
3733 determine the viability of this alternate model.
- 3734 5. It is possible that in addition to different ICC's per condition, variability may occur
3735 across sessions within condition, such that a range of ICCs exists. If that range is
3736 determined to be sufficiently wide, we will consider adding cluster-adjusted standard
3737 errors for both the fixed and random-effects. Note that this type of standard error is a
3738 generalization of the traditional sandwich estimator; StataCorp has provided a FAQ
3739 on this generalization with citations:
3740 http://www.stata.com/support/faqs/stat/robust_ref.html.

3741

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3747

3748 Additional Analyses

3749

3750 **Secondary Analyses in relation to the Secondary Aims and Hypotheses**

3751 In addition to the above analyses, we will conduct analyses necessary to support our secondary
3752 aims of the trial, as outlined below.

3753

3754 **Aim 2: Compare the effect of the intervention in children who made significant changes**
3755 **in their dietary and/or physical activity behaviors to the effect in children who did not.**
3756 Hypothesis 2: Relative to children in the control condition, children participating in the treatment
3757 condition will:

3758 2.1 Have lower sedentary activity levels (as measured by actigraphy data) after the intensive
3759 phase of the intervention (T2) and at study completion and/or

3760 2.2 Have better adherence to age-specific USDA nutrition recommendations, (e.g., age-
3761 appropriate total calories increased, fruits and vegetables, decreased sugar sweetened
3762 beverages [measured via diet recall data]), after the intensive phase (T2) and at study
3763 completion.

3764

3765 **Analysis:**

3766 **(2.1)** A multiple regression model in which child sedentary activity level is regressed on group,
3767 controlling for baseline sedentary activity level and including other relevant covariates (e.g.,
3768 child gender), will be fit at T2 and at study completion.

3769 **(2.2)** Each child will be categorized as evincing, or not evincing, adherence to age-specific
3770 USDA recommendations (as defined in the hypothesis). This binary variable will be the outcome
3771 variable for this secondary analysis. We will test this first in an unadjusted analysis (a 2 x 2 table
3772 in which one variable is the outcome variable and the other is group [treatment or control]), and
3773 then in an adjusted logistic regression analysis predicting adherence category membership and
3774 including appropriate covariates (e.g., gender, baseline BMI) in addition to group.

3775

3776 **Aim 3: Evaluate the effect of parents' physical activity levels and dietary behaviors on**
3777 **children's levels of the same.**

3778 Hypothesis 3: Parents who have significantly lower sedentary activity levels (compared to
3779 baseline) after treatment or who have better adherence to USDA nutrition recommendations
3780 (age-appropriate total calories increased fruits and vegetables, decreased sugar sweetened
3781 beverages [measured via diet recall data]) will be more likely than parents who have higher
3782 sedentary activity levels or who do not adhere to USDA nutrition recommendations to have
3783 children who will show

3784 3.1: Decreased sedentary activity levels post-treatment and

3785 3.2: Better adherence to USDA nutrition recommendations (as measured in 2.2, above).

3786

3787 **Analysis:**

3788 Two binary predictors will be created denoting whether parents have significantly lower
3789 sedentary activity compared to baseline (yes/no) and whether they have appropriate versus
3790 inappropriate dietary adherence (yes/no). These dichotomous variables will be entered into
3791 models as follows:

3792 **(3.1)** A multiple regression model will be fit at T2 and at study completion in which child's
3793 sedentary activity level is regressed on group, controlling for baseline child sedentary level, and
3794 including the parent dichotomous variables, and two two-way interactions between the parent
3795 variables and group (treatment or control) (and including other relevant covariates [e.g.,
3796 gender]).

3797 **(3.2)** A logistic regression model will be fit at T2 and at study completion in which the binary
3798 child adherence variable (see hypothesis 2.2) is regressed on group and including the parent
3799 dichotomous variables and two two-way interactions between the parent variables and group
3800 (treatment or control)

3801 (and including other relevant covariates [e.g., gender]).

3802

3803 **Aim 4: Explore the potential for developing new social networks and their effect on child**
3804 **nutrition and physical activity.**

3805 Hypothesis 4: Parents in the treatment group will develop new social networks and the strength
3806 of those social networks will be positively associated with reduced sedentary activity levels and
3807 improved dietary behaviors (measured as indicated above) among both parents and children.

3808

3809 **Analysis:**

3810 A social network analysis will be conducted to determine the strength and cohesion of parents'
3811 reported networks. The effect of these networks on parental and child sedentary activity levels
3812 and dietary behavior will be estimated. Social network analysis will be conducted using the
3813 software packages UCINET and In-Flow. UCINET will be used for entering and analyzing
3814 network data and, along with In-flow, for generating network measures and graphical displays.
3815 This data set will thus contain both network and attribute variables at the individual level of
3816 analysis. Applying standard statistical techniques (e.g., regression, logistic regression, etc.)
3817 these independent variables will be modeled with selected dependent variables. The analysis
3818 will examine the change in these social networks over time and their impact on the main
3819 outcomes of interest including: growth trajectories (children's BMI); body composition (child and
3820 adult), parenting practices (child feeding); physical activity (child and adult), and total energy
3821 intake. The social network hypothesis suggests that members of a given network group will
3822 share health behavior characteristics more than members of other groups.

3823

3824 **Aim 5: Evaluate the moderating relationship between genetic risk factors and child BMI**
3825 **trajectories over the course of the study.**

3826 Hypothesis 5: Higher levels of child genetic susceptibility to obesity (i.e., a higher genetic risk
3827 score (Kathiresan, Voight et al. 2009)) will be significantly associated with heavier-for-age BMI
3828 at baseline, and this susceptibility will moderate children's growth in BMI over time.

3829

3830 **Analysis:**

3831 "Heavier-for-age-BMI at baseline", the outcome, will be regressed on genetic risk score and the
3832 interaction between risk score and time, controlling for other covariates as deemed important
3833 (e.g., child gender, etc.).

3834

3835 **Aim 6: Assess the degree to which implementation of the GROW program encourages**
3836 **additional lifestyle programming for preschool children and their parents in the Metro**
3837 **Community Centers.**

3838 Hypothesis 6: The two Metro Community centers participating in the GROW trial will implement
3839 a higher number of activity or nutrition programs for families (as defined by the centers) with
3840 young children at the end of the study compared to the number they implemented at baseline,

3841 and they will also implement a higher number after the study compared to the number
3842 implemented by non-participating Metro Community Centers.

3843

3844 **Analysis:**

3845 A simple count of the number of activity and nutrition programs will be taken at baseline within
3846 both Community Centers (i.e., East and Coleman) and then again at the end of the study to
3847 determine whether the number at study end within each center exceeds that at baseline.

3848 Similarly, counts will be taken of these types of programs at non-participating Metro Community
3849 Centers at baseline and study end and these numbers will be compared to counts at both East
3850 and Coleman to determine if both participating centers have higher numbers than the non-
3851 participating centers at baseline and at study end.

3852

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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	<ol style="list-style-type: none"> 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	<ol style="list-style-type: none"> 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	<ol style="list-style-type: none"> 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	<ol style="list-style-type: none"> 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	<ol style="list-style-type: none"> 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	<ol style="list-style-type: none"> 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

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3985

3986 **Original Statistical Analysis Plan**
3987 **Reviewed and approved by the DSMB in April, 2012**
3988

3989 $BMI = \beta_0 C + \beta_1 I + \beta_2 (age-X)C + \beta_3 (age-X)^2 C + \beta_4 (age-X)I + \beta_5 (age-X)^2 I + \dots + \text{error terms}$

3990 where:

3991 “I” is an indicator for group and equals 1 for the intervention group and 0 for the control group;

3992 “C” is an indicator for group and equals 1 for the control group and 0 for the intervention group;
3993 there is no intercept in this model in the ‘traditional sense’ (see point 2 below);

3994 “X” is the value at which we center age; we plan to use age at enrollment as our centering term,
3995 which will make the indicator variables interpretable (β_0 as the mean BMI at enrollment for those
3996 in the control group and β_1 as the mean BMI at enrollment for the intervention group);

3997 “...” stands for other predictors; at the present time, we believe that the predictors for the main
3998 model will be gender (coded, e.g., as 1 for female and 0 for male) and ethnicity (we expect there
3999 to be 3 ethnicity groups and thus 2 indicator variables for these); in addition, gender by age
4000 interaction terms will be included, since the literature indicates that trajectories may differ by
4001 gender;

4002 For the primary analysis, "error terms" will include subject, subject X age, and the covariance
4003 between these random effects, using a heterogeneous variance structure for the fitted model
4004 (Roberts & Roberts, 2005). For the primary analysis, we will not include a random effect for
4005 subject X age², given that, with our proposed unstructured covariance matrix, the inclusion of
4006 this additional random effect would result in 13 random-effects components and may lead to
4007 convergence problems (see Rabe-Hesketh & Skrondal, 2012, page 348). We will examine the
4008 consequences of this choice via planned secondary analyses.

4009 A post-hoc test of whether $\beta_3 = \beta_5$ will allow us to examine whether the quadratic terms differ
4010 between arms of the trial, thus answering our primary research question.

4011

4012 Interpretation of some terms: the indicator variable for trial arm, the linear term (age) for trial
4013 arm, and the quadratic term (age)² for trial arm jointly describe the trajectory (and starting point)
4014 for each group (intervention and control), and each can be interpreted as follows: the constant is
4015 the mean BMI at age on entry into the trial; the linear term indicates the rate of change at entry
4016 age; and the quadratic term indicates change in rate of growth (acceleration). In our
4017 specification, this model allows each child to have her/his own BMI intercept at baseline and
4018 own BMI trajectory. Accordingly, we do not include BMI at baseline as a predictor in our model.
4019 Additionally, we do not include a BMI by treatment interaction, because BMI is an outcome and
4020 treatment is a predictor. We plan to examine a baseline BMI by treatment interaction (as well as
4021 other interactions) in our secondary analysis.

4022

4023 Our hypothesis is that β_5 , the quadratic term for the intervention group, will be significantly
4024 different from β_3 , the quadratic term for the control group, at the 0.05 level. We do not have an

4025 hypothesis about the linear terms. Note that we expect the sign of β_5 to be positive, and we
4026 expect the coefficient to be smaller than the coefficient for β_3 .

4027

4028 ***Final Statistical Analysis Plan***
4029 ***Finalized in November, 2016***
4030

4031 Study Design

4032 The design of the study is a longitudinal non-blinded (open) randomized control trial. Within
4033 each of two sites, adult-child dyads with children ages 3-5 years will be randomly assigned,
4034 stratified according to parent language use (English or Spanish), to either the three-year
4035 prevention program or the control condition. Assessments will occur over 6 time points within
4036 each cohort, beginning at baseline and including assessments post-intervention (at 12 weeks/3
4037 months), and at 9, 12, and 36 months from baseline.

4038

4039 Primary Research Question and Hypothesis

4040 Our primary research question is about the impact of the GROW trial on the growth rate of
4041 children's BMI over time. Specifically, we hypothesize the following:

4042 Hypothesis 1: The BMI trajectories of children in the treatment group will change at a slower
4043 rate than those in the control group over time.

4044

4045 Primary Outcome

4046 Although childhood obesity is a well-documented public health concern, most studies have
4047 assessed the obesity outcome (e.g., BMI) using only a single time point or incorporating a pre-
4048 post design, leaving us with little knowledge about the actual shape or growth rate of trajectories
4049 of BMI during this critical period of development. Indeed, few studies have taken a
4050 developmental perspective in order to understand how and when obesity develops in early
4051 childhood. By measuring BMI at multiple time points, we will examine growth trajectories in early
4052 childhood.

4053 * * *

4054 Because clinical literature about childhood obesity indicates that the shape of the BMI trajectory
4055 across ages 3 to 8 is curvilinear, we will account for this in our analytic plan. ([Kuczmarowski, Ogden
et al. 2002](#); [Cole 2004](#)) (see below).

4057

4058 Primary Analysis

4059

4060 Statistical model and approach

4061

4062 Our primary analysis will be an intent-to-treat analysis, and we will fit a multilevel mixed-effects
4063 linear model using a maximum likelihood procedure to handle missing data.

4064 Time-varying BMI will be the outcome at Level 1 nested within children at Level 2. Time at
 4065 Level 1 will be in years since baseline as computed from the date of each child's measurement
 4066 at each time point. The following child-level (Level 2), time invariant variables will be predictors
 4067 of the linear and quadratic BMI growth rates and the intercept at Level 1: age at baseline
 4068 (centered at a value of interest) and random assignment to intervention or control. Child gender
 4069 will be a child-level (Level 2), time invariant predictor of the intercept at Level 1. This approach
 4070 allows the estimation of growth rates based on each child's individual measurement dates, and
 4071 accounts for both age at baseline and time in the study.

4072 The Level 1 equation is as follows:

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

4073 where BMI for each child i is repeated over time t . BMI for a given child is a function of the
 4074 individually varying baseline intercept π_{0i} , the linear growth rate π_{1i} across 36 months, the
 4075 quadratic growth rate (acceleration) π_{2i} , and a random error term.

4076

4077 The intercept and two growth parameters will then be regressed on Level 2 (child-level)
 4078 predictors as follows:

4079 BMI Intercept: $\pi_{0i} = \beta_{00} + \beta_{01}(age - C)_i + \beta_{02}(I)_i + \beta_{03}(F)_i + r_{0i}$

4080 Linear Growth: $\pi_{1i} = \beta_{10} + \beta_{11}(age - C)_i + \beta_{12}(I)_i + r_{1i}$

4081 Quadratic Growth: $\pi_{2i} = \beta_{20} + \beta_{21}(age - C)_i + \beta_{22}(I)_i + r_{2i}$

4082 where I is an indicator for group assignment and equals 1 for the intervention group and 0 for
 4083 the control group, and F is an indicator for sex and equals 1 for females and 0 for males. β_{00} is
 4084 the mean initial BMI in control group males while adjusting for child age at baseline (centered),
 4085 β_{01} is the effect of child age at baseline (centered) on initial BMI, β_{02} is the effect of being
 4086 assigned to the intervention group on initial BMI (expected to be 0), β_{03} is the effect of being
 4087 female on initial BMI, and r_{0i} is the random error variance. β_{10} represents the linear growth rate
 4088 at baseline in the control group while adjusting for child age at baseline, and β_{11} is the effect of
 4089 child age at baseline on linear growth. β_{12} is the intervention effect on linear growth, and β_{22} is
 4090 the intervention effect on BMI acceleration while adjusting for child age at baseline.

4091 The Level 1 and Level 2 equations can then be combined and regrouped to yield a single
 4092 equation for the model:

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

4093 where the terms in the first bracket contribute to the intercept, the second bracket's terms
 4094 contribute to the linear growth, the third bracket's terms contribute to the quadratic growth, and
 4095 the final bracket contains all of the random error terms. We will specify an unstructured
 4096 variance-covariance matrix.

4097 We will conduct a likelihood ratio test with two degrees of freedom to test whether the linear and
4098 quadratic intervention effects (β_{12} and β_{22} , respectively) are jointly equal to zero. If this joint test
4099 is not significant at $p < 0.05$ then intervention effectiveness is not demonstrated. If this joint test
4100 is significant at the $p < 0.05$ level, then the intervention effect was significant.

4101

4102 Missing data including level of attrition, lost to follow-up, and missing data treatment

4103 With 6 repeated measurements, some participants inevitably will miss one or more occasions of
4104 outcome data collection. One advantage of the mixed models over older repeated measure
4105 ANOVA models is the use of all available data without dropping any subjects ([Nich and Carroll
4106 1997](#)).

4107

4108 References

4109 Singer, J.D., & Willett, J. B. (2003). Applied longitudinal data analysis: Modeling change and
4110 event occurrence. New York, NY: Oxford University Press.

4111 Harold, G. T., et al. (2013). Depressive symptom trajectories among girls in the juvenile justice
4112 system: 24-month outcomes of an RCT of multidimensional treatment foster care. *Prev. Sci.*
4113 (14). DOI: 10.1007/s11121-012-0317-y.

4114

4115

4116 **Summary of Primary Analysis Adjustments, Clarifications and Specifications**
4117

4118 All changes were made with all study personnel still blinded to non-baseline data aggregated by
4119 group, including the site-statisticians.

4120 The original analysis plan specified what we thought the predictor variables would be at the
4121 time. We have now finalized the included predictor variables for the primary analysis plan. We
4122 still adjust for age at baseline and gender, but we do not adjust for ethnicity because of the
4123 relative homogeneity of our recruited sample.

4124 Gender is a predictor of the intercept (i.e., initial BMI), and we no longer include a gender by
4125 age interaction. This is because the literature shows that girls have a lower BMI intercept than
4126 boys at a given age, but the overall shapes of their respective growth curves are comparable.

4127 The revised plan has clarified that the age predictor is baseline age, and time is longitudinal
4128 follow-up representing the time a child was exposed to the intervention or control.

4129 The original plan specified that post-hoc secondary analyses would be conducted to determine
4130 the potential effect of using different methods for handling missing data (e.g., multiple imputation
4131 [MI] with and without auxiliary variables), and we still plan to do this. The current plan makes it
4132 clear that we will be using a maximum likelihood (ML) procedure to handle missing data in the
4133 primary analysis.

4134 The original primary hypothesis was that the quadratic term for the intervention group will be
4135 different from the quadratic term for the control group at the $p < 0.05$ level. There was no
4136 hypothesis for the linear term. In the current plan we will conduct a likelihood ratio test with two
4137 degrees of freedom to test whether the linear and quadratic intervention effects are jointly equal
4138 to zero. Intervention effectiveness will be demonstrated if this joint test is significant at the
4139 $p < 0.05$ level. We made this change because both the linear and quadratic terms determine the
4140 overall shape of the outcome curve, and this approach is consistent with typical growth
4141 modeling (Singer & Willett, 2003). It is critical to note again that this determination was made
4142 with all study personnel blinded to non-baseline data aggregated by group, including the site-
4143 statisticians.

4144 The original analysis plan proposed a heterogeneous variance structure, allowing for the ICC at
4145 the level of session to be estimated separately for the intervention arm and not for the control
4146 arm (because control participants are not assigned to group sessions). We have since decided
4147 to model a homogeneous variance structure in the primary analysis; we will explore for a
4148 potential heterogeneous variance structure in secondary analyses.

4149