Revision History of this Protocol Template:

Version Information	Summary of Revisions Made	Rationale
Version 2.0 – Approved by Principal Investigator, Co-Investigators and Consultants	Expanded ages of children to 3 to 5 years old	To increase the study sample

Healthy Mothers-Healthy Children

Protocol Number:

National Clinical Trial (NCT) Identified Number: NCT03866902 (March 7, 2019)

Principal Investigator: Dr. Hudson Santos

Sponsor: The National Institute of Nursing Research

Grant Title: Healthy Mothers – Healthy Children: An Intervention with Hispanic Mothers and their Young Children

Grant Number: 1R01NR017199-01

Funded by: The National Institute of Nursing Research

Version Number: 2

2019-06-19

Summary of Changes from Previous Version:

Affected Section(s)	Summary of Revisions Made	Rationale
Sample	Changed age of children from 4 year old to 3 to 5 year olds	To increase sample age range

CONFIDENTIALITY STATEMENT

This document is confidential communication. Acceptance of this document constitutes agreement by the recipient that no unpublished information contained herein will be published or disclosed without prior approval of the Principal Investigator or other participating study leadership and as consistent with the NIH terms of award.

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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

Principal Investigator or Clinical Site Investigator:

Signed:  Date: 2019-06-19

Name: Dr. Hudson Santos

Title: Principal Investigator

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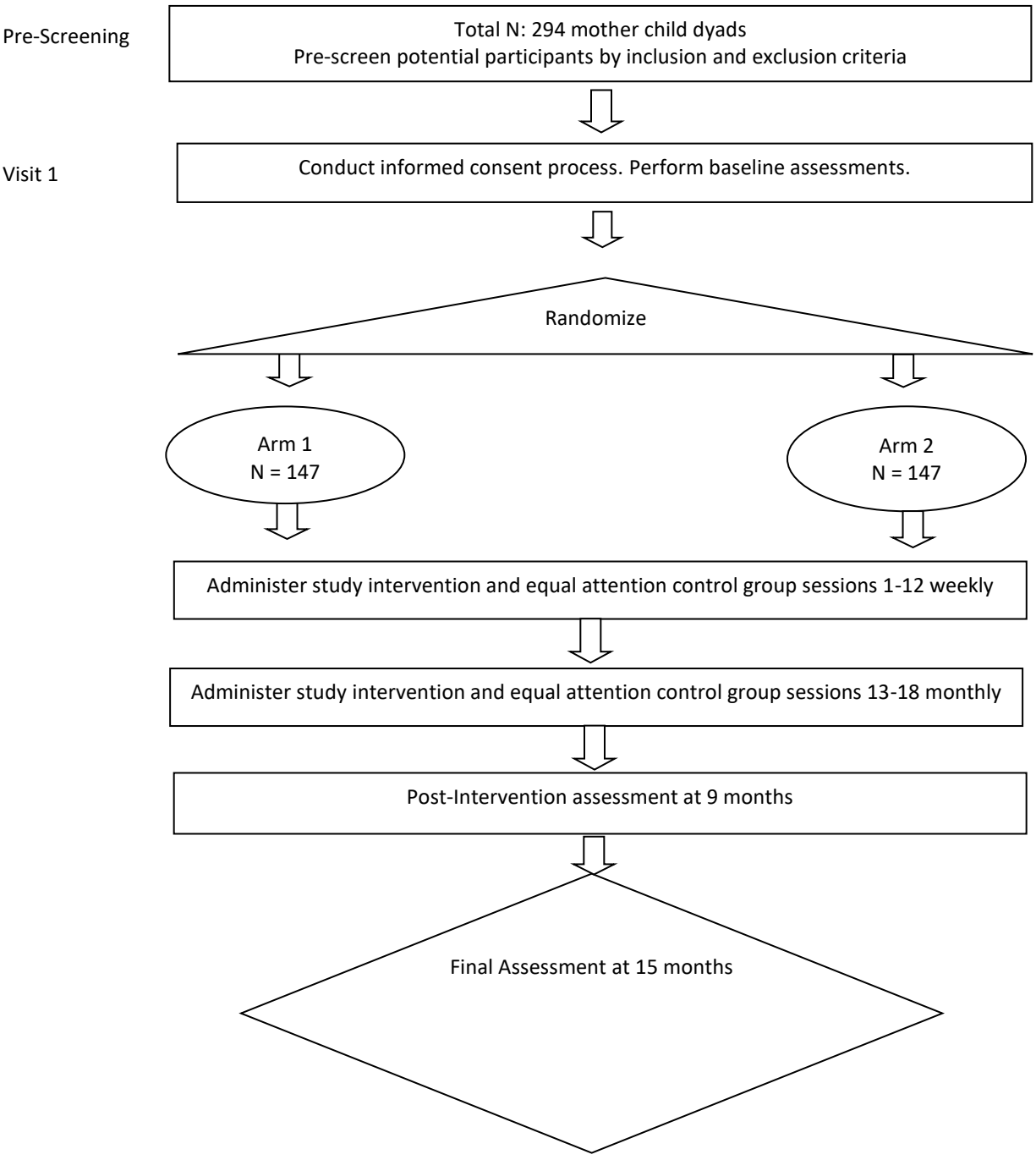
1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Healthy Mothers-Healthy Children: An Intervention with Hispanic Mothers and their Young Children
Grant Number:	1R01NR017199-01
Study Description:	This study will use a two-group randomized repeated measures study design to evaluate the efficacy of the intervention with 294 dyads of overweight or obese Hispanic mothers and their 3-5 year old children.
Objectives:	Primary Objectives: Adiposity and weight in mothers and children from Time 1 (baseline) to Time 2 (9 months) and Time 3 (15 months). Secondary Objectives: Health behaviors in mothers and children from Time 1 (baseline) to Time 2 (9 months) and Time 3 (15 months).
Endpoints:	Primary Endpoint: Adiposity and weight in mothers and children from Time 1 (baseline) to Time 2 (9 months) and Time 3 (15 months). Secondary Endpoints: Health behaviors in mothers and children from Time 1 (baseline) to Time 2 (9 months) and Time 3 (15 months).
Study Population:	A total of 294 Hispanic mothers and 294 Hispanic 3-5 year old children from two counties in North Carolina.
Phase or Stage:	Randomized controlled trial with an experimental and equal attention control group.
Description of Sites/Facilities Enrolling Participants:	Two public health departments and two community health centers in two counties in North Carolina. A total of 294 mothers and their 294 children ages 3-5 years old.
Description of Study Intervention/Experimental Manipulation:	An experimental group of women receive a nutrition, exercise and coping skills training and physical activity intervention. An experimental group of children receive Color Me Healthy classes. An equal attention control group women receive English for Second Language classes and the children have books read to them and they color with crayons.
Study Duration:	A total of 5 years or 60 months.
Participant Duration:	Each participant will be in the study a total of 15 months.

1.2 SCHEMA

Flow Diagram



1.3 SCHEDULE OF ACTIVITIES

Variables and Their Measurement	Respondent	Time 1	Time 2	Time 3
Short Acculturation Questionnaire for Hispanics	Mother	X		
Health History Questionnaire	Mother	X		
Sports Physical	Mother	X		
Adiposity (Primary Outcomes)				
Waist Circumference	Mother/Child	X	X	X
Triceps and Subscapular Skinfolds	Mother/Child	X	X	X
Weight Status (Primary Outcomes)				
Height/Weight	Mother/Child	X	X	X
BMI/BMI Percentile	Mother/Child	X	X	X
Health Behavior				
Adult Health Behavior Survey	Mother	X	X	X
Health Promoting Lifestyle Profile II	Mother	X	X	X
24-hour Food Recall for 3 days	Mother for Self/Child	X	X	X
Accelerometer for 7 days	Mother for Self/Child	X	X	X
Self-Efficacy				
Eating Self-Efficacy Scale	Mother	X	X	X
Exercise Self-Efficacy Scale	Mother	X	X	X
Demographic Data	Mother for Self/Child	X		
Health History Update Questionnaire	Mother for Self/ Child		X	X
Process Evaluation Bi-Monthly	Project Manager			
Exit Interviews	Mother			X

Time 1 (0 months [baseline])

Time 2 (9 months [completion of the intervention])

Time 3 (15 months [after 6 months with no contact from the study staff])

2 INTRODUCTION

2.1 STUDY RATIONALE

Background: Hispanic women and children who become overweight or obese are at risk for developing prediabetes, type 2 diabetes, and cardiovascular disease later in life. Interdisciplinary interventions which target Hispanic women and their 3-5-year old children to improve nutrition and physical activity behaviors, manage adiposity and weight in mothers, and prevent excessive adiposity and weight gain trajectory in their children offer promise to break the intergenerational cycle.

Methods: Using a randomized two-group, repeated measures experimental design, the goal of the proposed study is to investigate the efficacy of a 12-week nutrition and physical activity program including education, coping skills training, and home-based intervention in Hispanic women and their 3-5-year old children. The program includes 6 months of continued monthly contact to help overweight and obese Hispanic mothers and their children improve adiposity, weight (trajectory for children), health behaviors (nutrition and physical activity), and self-efficacy We will partner with two federally qualified health departments in Durham and Chatham counties, North Carolina to enroll participants. We will partner with community centers to deliver the intervention. A total of 294 Hispanic women with a BMI$\geq$25 kg/m^2 and 294 Hispanic 3-5-year old children with a $\geq$25th BMI percentile will be enrolled over 4 years and randomized to the experimental or equal attention control group. Data will be collected at Time 1 (0 months [baseline]) to Time 2 (9 months [completion of the intervention]) and Time 1 to Time 3 (15 months [after 6 months with no contact from the study staff]). Data collected will include adiposity in mothers and children and weight (primary outcomes: BMI in mothers and BMI percentile in the children). Secondary outcomes will include health behaviors and self-efficacy in the mothers and in the children. We will also evaluate the cost of delivering the program for public health departments. We will use general linear mixed models to test the hypotheses.

Discussion: Decreasing overweight and obesity in Hispanic women and slowing adiposity and weight gain trajectory in young Hispanic children is urgently needed to decrease morbidity, mortality, and future health care costs.

2.2 BACKGROUND

There is an urgent need to prevent excessive adiposity and weight gain trajectory in Hispanic children. Overweight (BMI $\geq$ 85th and < 95th percentile) and obesity ($\geq$ 95th percentile) are prevalent in both genders, affect all ages, and cross all ethnic groups, though minority children from families with lower incomes and less education are particularly high-risk [1]. The prevalence of overweight and obesity in 2-to-19 year old Hispanic youth is 38.9%, non-Hispanic Black youth is 35.2%, and non-Hispanic White youth is 28.5% [1]. Obesity increases risk for developing prediabetes, type 2 diabetes and cardiovascular disease [2, 3]. Childhood obesity is estimated to cost $14 billion annually in direct medical costs in the United States (U.S.) [4, 5].

There are currently 55.3 million Hispanics living in the U.S. [6]. In 2014, Hispanics accounted for 9% of the population in N.C. [6]. Overweight and obesity in Hispanic mothers and their children involve a complex interplay between acculturation, the food environment, the built environment, the influence of media, and a lack of support [7]. Many Hispanic men work long hours, while mothers stay home to care for their children without close family support [7]. Greater acculturation is significantly associated with increased consumption of fast foods and decreased moderate-to-high intensity exercise [8, 9]. Many communities where Hispanics live lack access to healthy affordable food and have only one-third as many supermarkets as other communities [10]. Confronted with an abundance of low cost, calorie-dense, high fat food, and limited access to fresh produce. Hispanics increase their intake of calories and fat and decrease their intake of fruits and vegetables [7, 11].

Transportation, infrastructure, and safety issues limit Hispanic mothers' and children's options for physical activity. Mothers engage in less physical activity than in their home country where most did not own cars, televisions, or computers and they were more likely to include physical activity in their everyday life [7, 11]. Hispanic parents also report barriers to their children's physical activity [12], including neighborhood safety and transportation problems [12]. Hispanic children (25.9%) are less likely than non-Hispanic White children (46.6%) to be involved in organized physical activity outside of school [12]. The media also contributes to the lack of healthy eating and physical activity. In 2015, advertisers spent more than $7.8 billion on restaurant, food, and beverage advertising targeting Hispanic households [13]. Hispanic children spend more time watching television than non-Hispanic White children (321 minutes per day versus 216 minutes) [14], and the number of hours spent watching television is positively associated with overweight and obesity [15, 16].

Mothers influence children's nutrition and physical activity behaviors by modeling health behaviors, structuring children's activities, and selecting content and portion sizes of meals ***[17-20]***. Mothers have more influence when children are in the preschool stage than in later stages of development ***[21]***. Four year olds are able to pay attention to activities, think in logical steps, have good language skills, run, jump, skip, and socially and emotionally they start to share, cooperate and take turns ***[22]***. We propose to teach mothers strategies to improve their own nutrition and physical activity behaviors, build their self-efficacy, and learn how to help their children eat healthier and increase physical activity. We will focus on 3-5-year-olds because our pilot work indicates that they are developmentally more prepared for intervention than younger children *[23]*.

Nutrition and physical activity programs used in the general population that were found to be most effective incorporated both behavioral and cognitive strategies and included parental involvement ***[19, 24, 25]***. To date, we have found no interventions that have been developed to help overweight or obese Hispanic mothers manage their weight and prevent excessive adiposity and weight gain trajectory in their young children using a culturally and language tailored intervention. We propose to test the efficacy of a nutrition and physical activity education, coping skills training, and physical activity intervention (Healthy Mothers-Healthy Children Intervention) tailored to Hispanic mothers and using an age-appropriate nutrition and physical activity intervention for their 3-5-year-old children (Color Me Healthy) ***[26]***. Coping skills training includes social problem solving, cognitive restructuring, assertiveness training and conflict resolution to improve self-efficacy ***[27-31]***. We will provide support as mothers they increase their self-efficacy and practice new nutrition and physical activity behaviors and help their children eat healthier and increase physical activity.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Risks to Human Subjects

Human Subjects Involvement, Characteristics, and Design

Institutional Review Board (IRB) approval was obtained from The University of North Carolina at Chapel Hill (UNC-CH). Using a randomized two-group, repeated measures experimental design, the goal of the proposed study is to investigate the efficacy of a 12-week nutrition and exercise education, physical activity, coping skills training, and home-based exercise intervention in Hispanic women and their 3-5-year old children and 6 months of continued monthly contact to help overweight and obese Hispanic mothers improve adiposity, weight, health behaviors and self-efficacy and their 3-5-year old children improve their adiposity and weight gain trajectory. We will partner with two federally qualified health departments in two North Carolina

counties to enroll Hispanic women and their 3-5-year old children and we will partner with community centers to deliver the intervention.

Inclusion criteria for mothers will be age 18 years or older; self-identification as Hispanic heritage; limited English proficiency and little acculturation, as measured by the Short Acculturation Scale for Hispanics with a score from 1.00 to 2.99; ability to understand spoken Spanish; a BMI >25kg/m_2; residence with the child; consent to join the study and consent for their child to join the study. Inclusion criteria for children will be age 3-5-years; ability to understand spoken Spanish; a BMI > 25th percentile for age and gender; and mother's consent for them to join the study. Health care providers will not be asked to give permission for either mothers or children to join the study. Mothers will fill out a health history questionnaire to ascertain if they have a heart murmur, congenital heart disease, family history of sudden death, difficulty walking or exercising or history of psychological problems that would prevent participation in group classes. A sports physical will be conducted by a bilingual nurse practitioner on all mothers during baseline data collection to ensure that they have no medical problems that would prohibit physical activity. If a mother answers yes to any of these health history questions or the nurse practitioner finds a heart murmur or any other concerns, she will be excluded from the study and referred to a health care provider. Dyads will be enrolled in eight cohorts over four years. Each cohort will be enrolled over a 1-month period. We have not included fathers, as in previous studies in this population we have learned the majority of these fathers work 6 days a week and do not have the time to attend class with their child. After enrollment and baseline assessment, dyads will be randomized to either the intervention or control group using a computer-generated randomization table, stratifying by BMI group, overweight (<30 kg/m_2) and obese (>30kg/m_2), and utilizing blocking to help ensure balance between the groups. Mothers will be informed of their group assignment by telephone.

Data will be collected at Time 1 (Baseline [0 months]), Time 2 (Post Intensive Intervention and Continued Support [9 months]), and Time 3 (6-Months after Completion of Continued Support [15 months]). Data collected will include adiposity (primary outcome) in mothers and children (waist circumference, triceps and subscapular skinfolds), weight status (primary outcome) in the mothers (body mass index [BMI]) and BMI percentile in the children, health behaviors in the mothers (Adult Health Behavior Questionnaire, Lifestyle Health Promoting Profile II, 3 day 23-5-Hour Food Recall, and 7 day Accelerometer) and in the children (3 day 24-Hour Food Recall and 7 day Accelerometer). Self-Efficacy in the mothers (Eating Self-Efficacy Scale and Exercise Self-Efficacy Scale) will also be measured. We will also evaluate the cost of delivering the program for public health departments. Data analysis will use general linear mixed models to test the hypotheses. Both intervention and control group mothers will each receive $50 after each data collection and $5 each time they come to class or data collection to help with transportation costs.

The mothers in the Healthy Mothers-Healthy Children Intervention group will receive a 12 week Intensive Intervention and 6 months of Continued Support. The Intensive Intervention will include 60 minutes of nutrition and exercise education and coping skills training and a 45 minute physical activity class and a home-based physical activity program each week for 12 weeks. The Continued Support classes for the mothers in the intervention group will include 60 minutes of classroom discussion regarding problems they are having with nutrition and physical activity for themselves and their children and a 45 minute physical activity class monthly for 6 months. The children in the intervention group will receive an Intensive Intervention (105 minutes total), which will include 60 minutes of Color Me Healthy classes and 45 minutes of free play weekly for 12 weeks. The Continued Support classes for the intervention children will include a review of the Color Me Healthy classes and 45 minutes of free play monthly for 6 months. Each weekly or monthly class for mothers and children is a total of 105 minutes.

The equal attention control group mothers will receive English as a Second Language (ESL) classes for 105 minutes for 12 weekly classes and then monthly classes for 6 more months. The equal attention control group mothers will receive homework assignments to help them practice their English language skills. The homework handouts will be at the same frequency as the Healthy Mothers-Healthy Children Intervention group

mothers. The equal attention control group children will receive 105 minutes of free play for 12 weekly classes and then 6 monthly free play classes.

Participants will be tracked using ID numbers. All data will be double entered by different RAs into a SAS database with built-in range checks and skip patterns. Comparisons will be run on the two versions, and inconsistencies will be checked against the raw data and corrected. Data will be verified and stored in a secure server. Data will undergo range, consistency, and outlier checks. All data decisions will be recorded in a logbook with an audit trail. SAS datasets will be created for analysis.

Risks to Human Subjects

The intervention requires that during the Intensive Intervention each intervention woman and child attend 12 classes for 60 minutes. During Continued Support women and children will meet monthly for 6 months with their interventionists. The interventionist will weigh all women in a private area and provide feedback. The interventionist will then meet with the women for 60 minutes to discuss nutrition and exercise challenges. The women will then attend a 45 minute exercise session. The women will also be encouraged to exercise 30 to 60 minutes a day on most days of the week. The equal attention control group women and children will receive an equal number of days and minutes to meet, however the mothers will receive English as Second Language classes and the children will receive free play.

As a part of the first data collection after the mothers consent for themselves and their child, the mothers will fill out data. A health history and sports physical will be conducted on all mothers during the baseline data collection to ensure there are no medical problems before engaging in physical activity. The mothers will also fill out a health history for their child. The sports physical will be conducted by a bilingual nurse practitioner hired for the study with experience in conducting sports physicals and medical clearance in a private room. At the data collection, the women will have their height, weight, waist circumference, triceps and subscapular skinfolds measured by a bilingual research assistant in a private room. Children will have their height, weight, waist circumference, triceps and subscapular skinfolds measured by a bilingual research assistant in a private room with their mother present. We are aware that adverse events may occur and an adverse event monitoring committee will monitor their occurrence and the overall risk of the study to both mothers and their children. Women who express fatigue during sessions will be excused from the session and another time convenient for them will be scheduled to make up the content. If a woman expresses fatigue during data collection, the data collection session will be terminated immediately, and a follow-up appointment scheduled. No adults expressed fatigue in Dr. Santos's previous studies. It is not anticipated that the classes or data collection will cause any adverse effects, but participants will be encouraged to identify any concerns to the study staff. Identifying data will be kept separate from questionnaires and locked in the PI's filing cabinets and locked office. All adult and child participants will continue to receive routine medical care from their health care providers throughout the study. Referral to their health care provider will be made if any adverse effects are self-identified There are no known social or legal risks for the women who consent to participate for themselves and consent for their children in this study.

Adequacy of Protection against Risks

We will hire only bilingual staff, and all recruitment and intervention materials and instruments will be in Spanish. Two months before enrollment, the bilingual project manager will give a presentation to staff at both public health departments and place Spanish language posters and brochures in each waiting room. The posters and brochures will describe the benefits of good nutrition and physical activity and state the eligibility criteria for study participation. We will also put ads in local Spanish language newspapers and announcements on the local Spanish language radio station with our toll free number. Bilingual RAs will be available in the waiting rooms on clinic days to share information about the study with mothers of Hispanic heritage. Face-to-face information classes worked well in our feasibility and pilot studies and we were able to

enroll a sufficient number of participants each week. If mothers are interested, the RAs will privately record their name and telephone number and schedule them for an enrollment screening telephone call.
We plan to enroll 10 mother-child dyads per week. However, we have built into the timeline additional time for enrollment for each cohort if needed. If we have any difficulty enrolling participants, we will work with both health departments and El Centro Hispano to provide advice and assistance. We will also seek the assistance of our Community Advisory Board, which will be made up of mothers of Hispanic heritage with a 3-5-year-old child.

The bilingual project manager will conduct a private telephone screening and ask mothers' height and weight and their child's gender, birthdate, height, and weight, calculate BMI for mothers and BMI percentile for children and ask the questions on The Short Acculturation Scale for Hispanics [52]. If both mother and child meet the study criteria, an appointment will be made to meet at the community center to confirm eligibility; the bilingual RAs will measure height and weight and confirm BMI and BMI percentile. If eligible, the RA will explain, in Spanish, the study, requirements of participants, and the risks and benefits of participating, and random assignment; and all questions will be answered. Only the mother and one 3-5 year-old child will be eligible to join the study. Childcare will be available for other children the mother brings with her in addition to her 3-5-year-old child. Data collection with mother-child dyads will occur in the morning or early afternoon when the mother's older children will be in school. Physiological data collection will be done in a private room. Bilingual RAs will collect the following data in the same order: health history questionnaire, sports physical, height, weight, waist circumference, triceps and subscapular skinfolds. The mothers will fill out their questionnaires in a group with a bilingual RA who will read all questionnaires in Spanish. Data collection will take 75 minutes for each mother-child dyad. We have extra time in the schedule for make-up data collection
At the time of data collection, women will have clinical data collected and will be asked to fill out data forms. A sports physical will be conducted on all mothers during the baseline data collection to ensure there are no medical problems before engaging in physical activity. The sports physical will be conducted by a bilingual nurse practitioner hired for the study with experience in conducting sports physicals and medical clearance in a private room. The clinical measurements and data forms should take approximately 75 minutes to complete. Women will be encouraged to self-identify any concerns to the study staff. There will be adequate time for women to ask questions, and they will be given phone numbers to reach the PI and project manager if they have any further questions or concerns

Confidentiality will be protected through a coding mechanism. The names of all participants will be removed from the data and a code number assigned. Each participant's identifying data will be separated from the study data, and the key identifying code numbers and the participant's identification will be kept by the PIs in a locked file cabinet in a locked office that only the PI and the project manager will have access to. Data will be reported in aggregate form without identifying information by site or individual. All research study personnel will be trained in IRB and HIPAA guidelines to maintain the security and confidentiality of the data. Mothers will be made aware of the precautions that the research team will take in keeping their data confidential. All identifying information will be destroyed at the earliest possible time following completion of the study. Publications arising from the study will not contain personal information. All data will be analyzed by groups, with no potential for individual participants to be identified.

2.3.2 KNOWN POTENTIAL BENEFITS

Potential Benefits of the Proposed Research to Human Subjects and Others

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The major potential benefit of this study is the provision of new knowledge about ways to improve outcomes for women of Hispanic heritage with limited English proficiency and their 4-year old children. The intervention women will receive valuable information about nutrition and physical activity education, coping skills training, and physical activity. Their 4-year old children will receive valuable nutrition information and have an opportunity for physical activity. The equal attention control group will receive English as Second Language classes and the equal attention control group children will receive free play while their mothers are in class. Collection of data on mother's weight, adiposity, health behavior, and self-efficacy and children's weight and adiposity outcomes should provide information for women to share with their health care providers regarding efforts they are making to improve health behaviors in themselves and with their children.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

See 2.3.1 above for assessment of potential risks and benefits

3 OBJECTIVES AND ENDPOINTS

Aim 1: Test the efficacy of the intervention in slowing adiposity and weight gain trajectory and improving health behaviors (nutrition and physical activity) in 3-5-year-old Hispanic children from Time 1 (0 months [baseline]) to Time 2 (9 months [completion of the intervention]) and Time 1 to Time 3 (15 months [after 6 months with no contact from the study staff]).

Aim 2: Test the efficacy of the intervention in decreasing adiposity and weight and improving health behaviors and self-efficacy in overweight or obese Hispanic mothers from Time 1 to Time 2 and from Time 1 to Time 3.

Primary outcomes include slowing of child adiposity (waist circumference and triceps and subscapular skinfolds) and weight gain (BMI percentile) trajectory and a decrease in mother's adiposity and weight (BMI). We hypothesize that intervention group children will slow the trajectory of adiposity and weight gain and intervention group mothers will decrease adiposity and weight significantly more than the control group.

Secondary outcomes include child and mothers health behaviors (nutrition and physical activity) and mother's self-efficacy (nutrition and physical activity). We hypothesize that intervention group children and mothers will improve health behaviors and mothers will improve self-efficacy significantly more than the control group.

Aim 3: Identify the mediators through which the intervention influences the trajectory of adiposity and weight gain in children and decrease in adiposity and weight in mothers. We hypothesize that health behaviors and self-efficacy may mediate adiposity and weight loss in mothers and nutrition and physical activity behaviors in children may mediate a slower adiposity and weight gain trajectory.

Aim 4: Calculate the cost of implementing the intervention for public health departments and the costs for mothers participating, from Time 1 to Time 2 and compare these costs to the outcomes of the intervention (cost-effectiveness) and the potential economic benefits of these outcomes (cost-benefit analysis). We hypothesize that the intervention is primarily focused on knowledge and behaviors in an at-risk population and may be cost-effective in comparison with other approaches to managing overweight and obesity.

Exploratory Aim: Determine whether intervention group mothers in the overweight versus obese BMI category benefit equally from the intervention in adiposity, weight, health behaviors, and self-efficacy.

4 STUDY DESIGN

4.1 OVERALL DESIGN

This study will use a two-group, randomized repeated measures study design to evaluate the efficacy of the intervention with 294 dyads of overweight or obese Hispanic mothers and their 3-5-year-old children. The mothers in the Healthy Mothers-Healthy Children Intervention group will receive a 12 week intensive intervention and 6 months of continued support. The intensive intervention will include 60 minutes of nutrition and exercise education and coping skills training and a 45 minute physical activity class and a home-based physical activity program handout each week for 12 weeks. The continued support classes for the mothers in the intervention group will include 60 minutes of classroom discussion regarding problems they are having with nutrition and physical activity for themselves and their children and a 45 minute physical activity class monthly for 6 months. The children in the intervention group will receive an intensive intervention (105 minutes total), which will include 60 minutes of Color Me Healthy classes [26] and 45 minutes of free play weekly for 12 weeks. The continued support classes for the intervention children will include a review of the Color Me Healthy classes [26] and 45 minutes of free play monthly for 6 months. Each weekly or monthly class for mothers and children is a total of 105 minutes. The equal attention control group mothers will receive English as a Second Language (ESL) classes for 105 minutes for 12 weekly classes and then monthly classes for 6 more months. The equal attention control group mothers will receive homework assignments to help them practice their English language skills. The homework handouts will be at the same frequency as the Healthy Mothers-Healthy Children Intervention group mothers. The equal attention control group children will receive 105 minutes of free play for 12 weekly classes and then 6 monthly free play classes.

Data will be collected at Time 1 (0 months [baseline]), Time 2 (9 months [completion of the intervention]) and Time 3 (15 months [after 6 months with no contact from the study staff]). Time 2 data will determine the magnitude of the intervention effects after the intensive intervention and continued support; Time 3 data collection will test efficacy after the mother-child dyads have had sufficient time to implement their new nutrition, physical activity, and coping skills on their own. These times were chosen because 3 to 6 months after completion of an intervention represents a standard length of time for follow-up in weight reduction studies, and gives mothers and children the time necessary to make changes in health behaviors [19].

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The study design will use a two-group randomized repeated measures study design to evaluate the efficacy of the intervention with 294 dyads of overweight or obese Hispanic mothers and their 3-5 year old children.

4.3 JUSTIFICATION FOR INTERVENTION

The intervention was pilot tested face-to-face in this population and was found to be feasible and acceptable.

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if she and her child has completed Time 1 (baseline), Time 2 (9 months) and Time 3 (15 months) data collection.

5 STUDY POPULATION

Settings. The study will build upon established partnerships between The University of North Carolina at Chapel Hill, the Chatham County Health Department and Durham County Health Department. Bilingual research assistants (RAs) will distribute brochures, give mothers information about the study, answer questions and enroll mother-child dyads. This approach worked well in previous studies [32, 33]. In 2015, the Chatham County Health Department provided 82,314 medical visits and 42% (34,572) were provided to Hispanic adults and children and the Durham County Health Department provided 78,123 visits and 46% (35,936) were provided to Hispanic adults and children. In 2015, the Durham County Health Department had 650 Hispanic mother and 4-year old child dyads and the Chatham County Health Department had 800 Hispanic mother and 4-year old child dyads (Total = 1,450; Mean = 725). A total of 78% of Hispanic mothers are overweight or obese [34]. Thus it is anticipated that approximately 78% of the mothers at both sites will meet inclusion criteria (n = 1,131), and 50% (n = 565) will agree to participate with their 4-year-old child. Of those who agree to participate (n = 565), approximately 70% (n = 396) will score a 1.00-2.99 on the Short Acculturation Questionnaire for Hispanics establishing low acculturation [35]. These numbers are adequate to meet our projected enrollment of 294 dyads. Specifically, we will enroll 36-38 dyads for each cohort in each site in each of eight rolling enrollment periods. We will rent space for the intervention from community centers in Chatham and Durham Counties as we have done in previous studies (see Letters of Support). The public health departments and community centers are situated in the communities where participants live and they are either within walking distance from their homes or on bus lines, increasing the probability of successful recruitment and retention for the proposed study. In previous studies, the mothers drove to the community centers together [23]. The centers have classrooms and playgrounds.

Sample. Inclusion criteria for mothers will be age 18 years or older; self-identification as Hispanic; limited English proficiency; little acculturation, as measured by the Short Acculturation Scale for Hispanics [35] with a score from 1.00 to 2.99; ability to understand spoken Spanish; a BMI $\geq$25kg/m^2; residence with the child; consent to join the study and consent for their child to join the study. Inclusion criteria for children will be age 3-5-years; ability to understand spoken Spanish; and a BMI $\geq$ 25th percentile for age and gender. Health care providers will not be asked to give permission for mother-child dyads to join the study. Mothers will fill out a health history questionnaire to ascertain if they have a heart murmur, congenital heart disease, family history of sudden death, difficulty exercising or psychological problems that would prevent participation. A sports physical will be conducted by a bilingual nurse practitioner on all mothers during baseline data collection to ensure that they have no medical problems. If a mother answers yes to any of these health history questions or the nurse practitioner finds a heart murmur or any other concerns, she will be excluded from the study and referred to a health care provider. Dyads will be enrolled in eight cohorts over four years. Each cohort will be enrolled over a 1-month period.

5.1 INCLUSION CRITERIA

Inclusion criteria for mothers will be age 18 years or older; self-identification as Hispanic; limited English proficiency; little acculturation, as measured by the Short Acculturation Scale for Hispanics [35] with a score from 1.00 to 2.99; ability to understand spoken Spanish; a BMI $\geq$25kg/m^2; residence with the child; consent to join the study and consent for their child to join the study. Inclusion criteria for children will be age 3-5-years; ability to understand spoken Spanish; and a BMI $\geq$ 25th percentile for age and gender.

5.2 EXCLUSION CRITERIA

Health care providers will not be asked to give permission for mother-child dyads to join the study. Mothers will fill out a health history questionnaire to ascertain if they have a heart murmur, congenital heart disease, family history of sudden death, difficulty exercising or psychological problems that would prevent participation. A sports physical will be conducted by a bilingual nurse practitioner on all mothers during baseline data collection to ensure that they have no medical problems. If a mother answers yes to any of these health history questions or the nurse practitioner finds a heart murmur or any other concerns, she will be excluded from the study and referred to a health care provider.

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Screen failures will not be consented or enrolled in the study. We will keep track of screen failures and reasons why they failed to meet inclusion criteria.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Procedures for Minority Recruitment and Enrollment and Challenges

We will hire only bilingual staff, and all recruitment and intervention materials and instruments will be in Spanish. Two months before enrollment, the bilingual project manager will give a presentation to staff at both public health departments and place Spanish language posters and brochures in each waiting room. The posters and brochures will describe the benefits of good nutrition and physical activity and state the eligibility criteria for study participation. We will also put ads in local Spanish language newspapers and announcements on the local Spanish language radio station with our toll free number. Bilingual RAs will be available in the waiting rooms on clinic days to share information about the study with Hispanic mothers. Face-to-face information classes worked well in our feasibility and pilot studies and we were able to enroll a sufficient number of participants each week [23]. If mothers are interested, the RAs will privately record their name and telephone number and schedule them for an enrollment screening telephone call. This technique also worked well in our pilot study, which included mother-child dyads with limited English proficiency [23]. Of 82 mother-child dyads approached in the pilot, 68% (n = 56) consented to participate over 1 month [23]. We plan to enroll approximately 10 mother-child dyads per week. However, we have built into the timeline additional time for enrollment for each cohort if needed. If we have any difficulty enrolling participants, we will work with both health departments to seek advice on how to improve enrollment in the study.

The bilingual project manager will conduct a private telephone screening and ask mothers' height and weight and their child's gender, birthdate, height, and weight, calculate BMI for mothers and BMI percentile for children and ask the questions on The Short Acculturation Scale for Hispanics [35]. If both mother and child meet the study criteria, an appointment will be made to meet at the community center to confirm eligibility; the bilingual RAs will measure height and weight and confirm BMI and BMI percentile. If eligible, the RA will explain, in Spanish, the study, requirements of participants, and the risks and benefits of participating, and random assignment; and all questions will be answered. Only the mother and one 3-5-year-old child will be eligible to join the study. Childcare will be available for other children the mother brings with her in addition to her 3-5-year-old child. Data collection with mother-child dyads will occur in the morning or early afternoon when the mother's older children will be in school. Physiological data collection will be done in a private room. Bilingual RAs will collect the following data in the same order: health history questionnaire, sports physical, height, weight, waist circumference, triceps and subscapular skinfolds. The mothers will fill out their

questionnaires in a group with a bilingual RA who will read all questionnaires in Spanish. Data collection will take 75 minutes for each mother-child dyad. We have extra time in the schedule for make-up data collection.

Procedures for Minority Retention and Challenges

Weight management studies typically have attrition rates ranging from 10%-30% [19]. To strengthen retention, our classes will be interactive, with culturally and linguistically tailored content developed to engage and sustain the interest of the mother-child dyads. Mothers who miss class will be offered a make-up class over the phone, and reminded when the next class will be held. Additional incentives will include childcare for other children who accompany mothers and their 3-5-year-olds to class and recipes and handouts in Spanish on how to improve their children's nutrition and physical activity behaviors. Mothers will be asked for telephone numbers of several family members and permission to call them if we cannot reach them. We will be as flexible as possible in scheduling enrollment and data collection appointments and provide tokens of appreciation such as birthday cards and a quarterly newsletter with updates on the study. Mothers in both groups will receive $25 after each data collection. These approaches proved successful in our pilot study with Hispanic mothers with limited English proficiency, where attrition was only 9%-15% [23] and those mothers who stopped coming had moved out of the state. We will make every effort to keep our attrition rate lower than the projected 15%. If retention rates drop below 85%, we will contact the mothers to ask why they stopped coming and develop strategies to meet the needs of each mother to assist them to continue in the study if possible.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION.

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

Intensive Intervention for Mothers

The intensive intervention classes are based on the classes from our Family Partners for Health study, adapted for Hispanic mothers with limited English proficiency and their 3-5-year-old children [23, 36, 37]. Classes will be run by a bilingual interventionist and will be 60 minutes long with 18-19 mothers. We chose 18-19 mothers since the enrollment is rolling and these mothers will be enrolled together and this cohort approach worked well in our previous studies [23, 37]. Classes will include nutrition and physical activity education and coping skills training using problem solving, assertiveness training, cognitive restructuring, and conflict resolution around problems of nutrition and physical activity for mothers and their children. The nutrition classes will include content on understanding calories, protein, carbohydrates and fat, making healthy substitutes that are culturally acceptable, choosing healthy foods when eating out at a favorite fast food restaurant, using actual menus, and understanding how portion control can make a difference for them and their children using food models and food labels in Spanish. Mothers will receive information on how to shop as economically as possible and how to shop at local farmers' markets, which are geographically close to the mother's homes, where they may have better access to fresh fruits and vegetables. At the end of each class, mothers will be asked to set a nutrition or physical activity goal for the coming week for themselves and their 4-year-old child.

Physical activity classes will be held for 45 minutes after the intensive intervention classes and will include a warm-up and then activities such as Zumba, Kick Boxing, walking, use of light weights and stretch bands, and a cool-down. The bilingual interventionist will reinforce the importance of physical activity and ways to increase physical activity for mothers and their children. The importance of decreasing sedentary behaviors for mothers and children will be reinforced in all classes. During the first week, each mother will receive a pedometer and log book for self-feedback. Mothers will be encouraged to bring their pedometer log book in weekly for the

bilingual interventionist to review. Pedometers will be used as a part of the intervention instead of a Fitbit because some of the women may not have a computer in their home to upload their data. Mothers will be encouraged to increase their physical activity weekly by small increments until they are physically active 30 to 60 minutes a day on most days of the week with their 3-5-year old child. Missed physical activity classes will not be made up. Mothers in the intervention group will be encouraged to develop their own home-based physical activity program using suggestions given in the physical activity class and a home-based physical activity handout in Spanish given after each physical activity class ti increase their and their child's physical activity. The handouts will be reviewed with the mothers and physical activities demonstrated by the bilingual interventionist.

Intensive Intervention for Children

The children's classes will include a 60 minute session plus 45 minutes of supervised free play with 18-19 children at the same time their mothers are in class. Each class will have 1 teacher and 3 teacher assistants to ensure safety. The Color Me Healthy [26] curriculum, which consists of 12 classes in Spanish, was purchased and used for the pilot study [23]. All of the classes are at a 3-5-year-old developmental level and include a CD with music and a song about the class of the week, colorful picture cards, and opportunities for the children to try new fruits and vegetables. Each week the bilingual interventionist will give mothers a Color Me Healthy [26] handout in Spanish that includes strategies for feeding their children healthier meals and snacks and increasing their daily physical activity. While their mothers are in physical activity class, the children will have 45 minutes of physical activity (supervised free play) in a playground at the community center or dance and actively play with the bilingual interventionist if it is raining.

Continued Support for Mothers and Children

During continued support, intervention mother-child dyads will return to the community center for classes once a month for 6 months. The mothers will receive a calendar at the completion of the intensive intervention classes with the dates and times and a reminder phone call several days before each class. As a part of the intervention, mothers will be weighed and then have the opportunity to engage in a discussion run by the bilingual interventionist, who will help mothers solve problems they have encountered related to nutrition and physical activity for themselves and their children for 60 minutes and then receive a 45 minute physical activity class. The children will meet with a bilingual interventionist to review a class from the Color Me Healthy ***[26]*** curriculum for 60 minutes and then receive 45 minutes of free play. If a mother and child miss a class, the bilingual interventionist will call and ask how the mother and child are doing and give the date of the next class. Continued support classes will not be made up.

Equal Attention Control Group

Mothers in the control group will receive English as a Second Language (ESL) classes taught by professional ESL teachers; they will receive the same number of contacts and time as the intervention group mothers (105 minutes weekly for 12 weeks and 105 minutes monthly for 6 months). The ESL classes will be offered because when exit interviews were conducted after the pilot study ***[23]***, mothers were asked if they "were not in the intervention group, what type of classes would they want?" The mothers (90%) wanted ESL classes to improve their English. Providing these classes to the control group most likely will improve enrollment and retention. Children in the control group will have free play while their mothers are in class and will receive the same number of contacts and times as the children in the intervention group (105 minutes weekly for 12 weeks and 105 minutes monthly for 6 months). The control classes will be held on separate days of the week from the intervention classes in the same community centers. Data will be collected from the mother-child dyads in the control group at Time 1, Time 2, and Time 3; and the mothers will receive $50 each time. Mothers will be called several days before classes and data collection to remind them. Mothers will receive a pedometer and log book after they

have completed Time 3 data. Attrition rates in our previous studies were equal in the intervention and control groups and ranged from 9% to 15% ***[23]***.

6.1.2 ADMINISTRATION AND/OR DOSING

See 6.1.1 for details

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

Fidelity of the Intervention

We have structured the fidelity of the intervention using the NIH five category Treatment Fidelity Framework [38]. For category one, **treatment design**, both the intervention and control condition will receive different content but will be the same length, number, and duration of contact over time. The bilingual interventionists will have experience teaching health interventions, and the theoretical model is clearly articulated. For category two, **training**, the bilingual interventionists will be trained by the PI and teach back the intervention to the PI. For category three, **delivery of the intervention**, integrity will be assessed by observation of two randomly selected classes per month by the project manager who will use a checklist to score classes based on pre-identified content, and drift will be defined as teaching less than 80% of protocol content. If drift occurs, the bilingual interventionists will be retrained until the protocol is followed consistently. We will also use a list of behavioral indicators to assess the interventionists' skills in facilitating classes, engaging mother-child dyads, role playing, problem solving, providing positive feedback, and goal setting. Retraining will be provided if problems are found. In our pilot study [23], we had little difficulty in maintaining consistency of the intervention. The bilingual interventionists will collect data on attendance at each class, reasons for non-attendance, and make-up classes provided. Category four, **receipt of treatment**, will be evaluated during the class by the bilingual interventionist who will assess understanding and answer all questions. Category five, **enactment of intervention skills**, will be evaluated during the six monthly continued support classes by the bilingual interventionist.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

After enrollment and baseline assessment, dyads will be randomized to either the intervention or control group using a computer-generated randomization table, stratifying by BMI group, overweight (25 – 29.9 kg/m^2) and obese ($\geq$30 kg/m^2), and utilizing blocking to help ensure balance between the groups. Mothers will be informed of their group assignment by telephone. We have not included fathers, as in previous studies in this population, because the majority of fathers work 6 days a week and cannot attend class ***[7, 23]***. Data collection research assistants will be blinded to group status.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

See 6.2.1 for details

6.5 CONCOMITANT THERAPY

N/A

6.5.1 RESCUE THERAPY

N/A

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

The intervention will only be discontinued after consultation with the study team and the program officer.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue a participant from the study for lost-to-follow up and unable to contact subject.

The reason for participant discontinuation or withdrawal from the study will be recorded. Subjects who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, and are randomized and receive the study intervention, and subsequently withdraw, or are discontinued from the study will not be replaced.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if she fails to return for scheduled visits and study staff are unable to contact the participant after at least 3 attempts.

The following actions must be taken if a participant fails to return for a required study visit:

The site will attempt to contact the participant, reschedule the missed visit, counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.

Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls. These contact attempts will be documented in the participant's medical record or study file.

Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Variables and Their Measurement	Respondent	Time 1	Time 2	Time 3
Short Acculturation Questionnaire for Hispanics	Mother	X		
Health History Questionnaire	Mother	X		
Sports Physical	Mother	X		
Adiposity (Primary Outcomes)				
Waist Circumference	Mother/Child	X	X	X
Triceps and Subscapular Skinfolds	Mother/Child	X	X	X
Weight Status (Primary Outcomes)				
Height/Weight	Mother/Child	X	X	X
BMI/BMI Percentile	Mother/Child	X	X	X
Health Behavior				
Adult Health Behavior Survey	Mother	X	X	X
Health Promoting Lifestyle Profile II	Mother	X	X	X
24-hour Food Recall for 3 days	Mother for Self/Child	X	X	X
Accelerometer for 7 days	Mother for Self/Child	X	X	X
Self-Efficacy				
Eating Self-Efficacy Scale	Mother	X	X	X
Exercise Self-Efficacy Scale	Mother	X	X	X
Demographic Data	Mother for Self/Child	X		
Health History Update Questionnaire	Mother for Self/ Child		X	X
Process Evaluation Bi-Monthly	Project Manager			
Exit Interviews	Mother			X

Time 1 (0 months [baseline]); Time 2 (9 months [completion of the intervention]); Time 3 (15 months [after 6 months with no contact from the study staff]).

8.2 SAFETY ASSESSMENTS

N/A

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

See Data Safety Monitoring (DSMP) Below

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

See DSMP Below

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

See DSMP Below

8.3.3.1 SEVERITY OF EVENT

See DSMP Below

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Data and Safety Monitoring Plan (DSMP)

Study Identification

NIH Study Number – 1R01NR017199-01

Study Title – Healthy Mothers: Healthy Children: An Intervention with Hispanic Mothers and their Young Children

Principal Investigator – Hudson Santos, PhD, RN

Study Overview

The overall goal of this project is to determine whether a nutrition and physical activity education, coping skills training, exercise program, and a home-based exercise program will decrease adiposity and weight, and improve health behaviors and self-efficacy in mothers of Hispanic heritage and slow excessive adiposity and weight gain in their 4-year old children. The DSMP outlined below for the proposed study will adhere to the protocol approved by The University of North Carolina at Chapel Hill (UNC-CH) Institutional Review Board (IRB) and the National Institutes of Health (NIH) and the National Institute of Nursing Research (NINR).

SECTION A. Monitoring Entity

Considering the study rationale, population, procedures, and the risk: benefit profile as outlined, the overall risk level for participation in this study is classified as no more than minimum risk.

1) Individual Roles and Responsibilities

An Executive Committee will be formed to oversee the conduct of the study. The committee will be comprised of nine members: Dr. Santos (Principal Investigator [PI]) and the Study Investigators, Drs. Ammerman, Crandell, Evenson, Faith, Peragallo-Montano, Perreira, Perrin, and Waters. The PI will Chair the Committee, which will meet monthly to review the activities of the study including management, personnel, recruitment, performance, and any emerging problems.

The Independent Monitor (ISM) for this study will be Dr. Mary Lynn. Dr. Lynn has been the Inaugural Assistant Director for Operations of the Office of Human Research Ethics at UNC-CH, which was preceded by six years as the IRB Chair and Chair of the School of Nursing (SON) IRB. Dr. Lynn is not associated with this research project and thus works independently of the PI. Dr. Lynn is not one of the key personnel involved in this grant. She is qualified to review the participant safety data generated by this study because of her unique expertise in human research ethics and serving as the ISM on multiple previous studies.

B. Procedures for Safety, Risk, and Confidentiality

1) Monitoring Study Safety

From the initial screening of participants by inclusion and exclusion criteria to the informed consent process to the provision of participant study instruction to staff training in Good Clinical Practices (GCP) and regulations pertaining to the Conduct of Human Participant Research to weekly contact with participants to internal monthly quality control audits and protocol fidelity monitoring to the real-time review of adverse events (AE) and serious adverse events (SAEs) by the PI, Study Investigators and the ISM, the study will be carefully oversighted.

Drs. Santos, Ammerman, Crandell (Study Statistician), Evenson, Faith, Lynn (ISM) Peragallo-Montano, Perreira, Perrin, and Waters will review the data for this study quarterly. We will examine participant accrual and adherence to the protocol regarding demographics and inclusion and exclusion criteria, and compliance of treatment, AE and SAE rates quarterly, and report regarding statistical power implications of dropouts and missing data annually.

Data on compliance to the intervention will be collected weekly by the Project Manager (PM) and reviewed quarterly by the Study Investigators, Study Statistician, and the ISM. Compliance on the part of participants will be evaluated by attendance and process evaluation as outlined in the study. If intervention attendance drops below 85%, the mothers who have stopped coming will be called to ask for feedback. Using information gained from these phone interviews, the PI will schedule a meeting with the Study Investigators and the ISM to discuss methods for improving compliance.

As in previous studies, the PI and the Study Statistician will oversight and train the PM to establish a system to ensure the verification of source data compliance. The source data will include original records necessary for the reconstruction and evaluation of the clinical trial. It will be clear who documented the data, documentation will be readable, signatures identifiable, contemporaneous, original copy, accurate and consistent, long-lasting and durable, available and accessible, complete, consistent, credible, and corroborated. All data will be first checked by two separate Research Assistants (RAs) at different times. REDCap will be used as our Research Electronic Data Capture System. The PI has been trained in REDCap and has used it in previous studies and REDCap is supported by UNC-CH. The REDCap database creation will be oversighted by Dr. Crandell (Study Statistician). Dr. Crandell will run comparisons and trained RAs will compare against source data and make corrections as needed. A data log book will be created to establish an audit trail for compliance as the PI has done in previous studies.

Drs. Santos, Ammerman, Crandell, Evenson, Faith, Peragallo-Montano, Perreira Perrin, and Waters will personally conduct and supervise the study. We will register the study in ClinicalTrials.gov. We will follow the protocol and ensure all study staff follow the protocol. All staff assisting with the study will be informed of their obligations. We will ensure informed consent, approval and reporting. We will report to the NIH/NINR Program Officer, Dr. Mary Roary, any AEs or SAEs. We will maintain adequate records and make them available for inspection. We will ensure initial and continuing review by UNC-CH IRB and will report all changes to research and involving risks to subjects, and not make any changes without IRB approval except where necessary to eliminate immediate hazards. All of the study team are CITI trained and follow the Good Clinical Practice (GCP) Guidelines.

2) Minimizing Research-Associated Risk

Diligent study safety monitoring will be conducted by the PI as follows. The PI will work with the IRB to set up a schedule of selected cases to ensure compliance with IRB requirements. The PI and Study Investigators have worked closely with the IRB in previous studies providing the data requested for audits as required. Risks to human subjects will be minimized through the utilization of establish protocols that have worked well in previous studies. We are aware that AEs and SAEs may occur and an Adverse Event Monitoring Committee will monitor their occurrence and the overall risk of the study to both mothers and their children.

Mothers who express fatigue during sessions will be excused from the session and another time convenient for them will be scheduled to make up the content. If a mother expresses fatigue during data collection, the data collection session will be terminated immediately, and a follow-up appointment scheduled. No mothers expressed fatigue in the PI's previous studies. It is not anticipated that the classes or data collection will cause any adverse effects, but participants will be encouraged to identify any concerns to the study staff. All mothers and their children will continue to receive routine medical care from their health care providers throughout the study. Referral to their health care provider will be made if any adverse effects are self-identified There are no

known social or legal risks for the mothers who consent to participate for themselves and consent for their children in this study. There will be adequate time for mothers to ask questions, and they will be given phone numbers to reach the PI and PM if they have any further questions or concerns.

Institution-Wide Assurances will be assured by the use of the protocol, which will be conducted fully in keeping with the signed PI in accordance with UNC-CH IRB, NIH, and NINR.

3) Protecting Confidentiality of Participant data Participant Screening and Enrollment

All data from participants screened for the study will be entered into the REDCap electronic study database. Designated research staff will collect, gather, and enter required data (written informed consent, Health Insurance Portability and Accountability Act (HIPAA) authorization, medical history and demographics) onto study data forms. Screened patients who do not meet study eligibility will have specific screening data entered into the study database. The collected data will be helpful in examining the patient population and feasibility of enrollment criteria and will include gender, age, race and reason for exclusion. All dates will be shifted and other Personal Health Information (PHI) will be removed from the study database upon study completion. All data obtained from this study will be used for research purposes only and will comply with Federal HIPAA regulations.

Written informed consent will be obtained from each participant at entry into the study. Informed consent is obtained by the following process. The participant will be read the study consent form in Spanish. The bilingual PM or trained bilingual RA will meet with the participant to review the form, to confirm the participant's understanding of the study, and to answer any questions that the participant might have. Once the participant demonstrates understanding of the study and agrees to participate in the study, the consent will be signed in the presence of the bilingual PM or bilingual RA. The IRB will oversight yearly renewal of consent forms and the PI and the research team will provide data as requested for the renewal.

Confidentiality will be protected through coding mechanisms. The names of all participants will be removed from the data and a code number assigned. Each participant's identifying data will be separated from the study data, and the key identifying code numbers and the participant's identification will be kept by the PI in a password protected computer in a locked office that only the PI and the PM will have access to. Data will be reported in aggregate form without identifying information by site or individual. All research study personnel will be trained in IRB and HIPAA guidelines to maintain the security and confidentiality of the data. Mothers will be made aware of the precautions that the research team will take in keeping their data confidential. All identifying information will be destroyed at the earliest possible time following completion of the study. Publications arising from the study will not contain personal information. All data will be analyzed by groups, with no potential for individual participants to be identified.

Case Report Forms. All proposed study specific case report forms (source documents) for data collection will be designed by the PI and PM in concert with the Study Statistician and transferred by the PM into electronic Case Report Forms (eCRFs) for use in the study's REDCap database. These study specific eCRFs source documents (study logs for correspondence, contacts, compensation and other forms such as pre-eligibility screens) will be coded by the participant's unique study identification number for all data collected including study instruments will be maintained in the participant research record that will be made accessible to study monitors. Completed instruments that require a signature on a paper CRF will be scanned and uploaded into the study database as well as maintained on file in accordance with UNC-CH policies and applicable Federal Regulations for the Conduct of Human Participant Research.

Binders. The PM will prepare and maintain a participant-specific binder for each participant containing all non-eCRFs records. A regulatory file will also be maintained to include the IRB approved Protocol, original

Informed Consent documents, HIPAA forms and other study-related regulatory documents. All paper research records and CRFs will be maintained in a locked file cabinet in a secure facility within the SON. Access to the research records, study database and PHI will be restricted to study personnel as approved by the PI and IRB. As with all studies conducted at the UNC-CH, this study is also eligible for a random audit by Office of Compliance.

Data Processing. This study will use Research Electronic Data Capture (REDCap) for data capture and management.

Data Security. Ensuring data security, compliance with 21 CFR 11 and maintaining the integrity of PHI is a top priority.

Data Entry. Each participant will be assigned a unique study identifier, all PHIs will be masked, and data exports will be limited to the PI, the PM, and Study Statistician for generating reports and the conduct of statistical data analysis.

Data Monitoring. Ongoing quality control procedures will be implemented for data collection, storage and processing. The PM will conduct monthly monitoring of the study database and generate a report for the PI to review at team meetings. Standing agenda items for these meetings will include participant recruitment and retention, AEs, SAEs, protocol deviations, data integrity and overall study conduct.

Database Protection. The REDCap database will be secured with password protection. The informatics manager receives only coded information, which is entered into the database under those identification numbers. Electronic communication with outside collaborators involves only unidentifiable information.

SECTION C. Procedures for Identifying, Reviewing and Reporting Adverse Events

1) Identifying. Potential risks identified for participants are outlined in the Protection of Human Participants and will also be outlined in the IRB approved informed consent document.

Dr. Mary Lynn (Chairperson of UNC-CH School of Nursing Human Participant Research Review Committee and ISM) will chair the Adverse Event Monitoring Committee, which will include Drs. Santos (PI), Ammerman, Crandell (Study Statistician), Evenson, Faith, Peragallo-Montano, Perreira, Perrin, and Waters and the PM. The committee will meet every 3 months or more often as warranted, to review data related to AEs and SAEs and assure that safety standards are maintained. Despite usual precautions, we are aware that AEs and SAEs may occur, and this committee will monitor their occurrence and the overall risk of the study to both mothers and their children. We will develop a system to test whether abnormalities are equally distributed between the intervention and equal attention control groups. Data will be presented to the committee if a significant increase in abnormalities is noted. The committee will be asked to establish measurable standards that must be met before they recommend modification of the study on the basis of safety. These standards will be clearly delineated in the meeting minutes and approved by the committee. The committee will provide the PI with recommendations regarding problems that would require modification for safety reasons. Minutes of each meeting will be kept, and all actions and decisions documented to establish an audit trail. Dr. Crandell, the Study Statistician, will be instructed by the PI to prepare the randomization plan for the study and prepare reports for the committee under the direction of Dr. Lynn (Chair and ISM).

2) Reviewing. Adverse events will be assessed and graded as follows.

Expected/Anticipated—Identified in nature, severity, or frequency in the current protocol, informed consent, investigator brochure, or with other current risk information.

Unexpected/Unanticipated—Not identified in nature, severity, or frequency in the current protocol, informed consent, investigator brochure, or with other current risk information.

More Prevalent—Occurs more frequently than anticipated or at a higher prevalence than expected.

Serious—Results in death, is life threatening, requires inpatient hospitalization or prolongs existing hospitalization, results in persistent or significant disability/incapacity, cancer, overdose, or causes a congenital anomaly/birth defect.

The relationship of AE to study participation will be determined by the Adverse Monitoring Committee as follows.

Unrelated—There is not a reasonable possibility that the adverse event may have been caused by the drug, device or intervention.

Possibly Related—The adverse event may have been caused by the drug, device, or intervention, however there is insufficient information to determine the likelihood of this possibility.

Related—There is a reasonable possibility that the adverse event may have been caused by the drug, device or intervention.

3) Reporting. The PI will responsible for ensuring that all AE and SAEs are reported to the NIH/NINR (Dr. Roary) and UNC-CH's IRB in compliance with their requirements.

Any AE will be reported by the PI to the Adverse Event Monitoring Committee within one week. An incident report will be created and sent by electronic email by the PI to Drs. Ammerman, Crandell (Study Staistician), Evenson, Faith, Lynn (ISM) Peragallo-Montano, Perreira, Perrin, and the PM. The PI will follow-up with the mother and child and will prepare a report. The AEs will be reviewed every three months and a report prepared for the Human Participants Committee and Dr. Roary at NIH/NINR. Process notes will be kept concerning any decisions.

Any SAE or deaths that occur during the study will be reported by telephone immediately to the Human Participants Research Review Committee Chairperson and Dr. Lynn (ISM) and to NIH/NINR (Dr. Mary Roary). An incident report will be sent by electronic mail by the PI to Drs. Ammerman, Crandell, Evenson, Faith, Peragallo-Montano, Perreira, Perrin, and the PM. The PI will follow-up immediately with the mother and child to investigate and prepare a report for all members of the Human Participants Committee and comply with all regulations regarding the reporting of SAEs. If the PI is unavailable, Dr. Perreira will be on-call in the PI's absence. The PI or Dr. Perreira in the PI's absence will be responsible for complying with all regulations concerning the reporting of a SAE and will prepare a full report for NIH/NINR. It is not expected that the committee will be involved in the decision to terminate the intervention for a study participant related to any adverse event. The PI will meet with the Study Investigators and the PM and seek input from the Program Officer (Dr. Mary Roary) and Dr. Lynn (ISM). Process notes will be kept concerning any decisions.

4) Examples of Potential Reportable Adverse Events. An AE is reportable is it meets all of the following criteria: 1) is unexpected 2) is related and/or possibly related, and 3) is serious and/or suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized. Additionally, per UNC-CH's policy all participant deaths, protocol deviations, complaints about the research, and breaches of confidentiality are reportable events.

An example of an AE would be that a 3-5-year old child decreases from the 25th percentile (normal or healthy weight) to below the 5th percentile (underweight) at the next data collection. The steps to be taken include withdrawing the child and their mother from the study. The PI will immediately contact Dr. Perrin (Pediatrician), Dr. Lynn (ISM), the IRB Contact person, and Program Officer Dr. Roary at NIH/NINR. The PI will assist the mother to call her Pediatrician and set up an immediate appointment to have her 4-year old child evaluated and ensure that follow-up was received.

An example of an SAE would be the death of a participant from acute renal failure, which although would be viewed as unexpected and unrelated to the intervention is nonetheless a reportable serious event. No further steps would be taken except to review, grade and report the event.

5) Safety Review Plan. Study progress and safety will be reviewed monthly (and more frequently if needed). Progress reports, including participant recruitment, retention/attrition, and AEs will be provided to Dr. Lynn (ISM) following each of the monthly reviews. An annual report will be compiled and will include a list and summary of AEs and SAEs. In addition, the annual report will address (1) whether adverse event rates are consistent with pre-study assumptions; (2) reason for dropouts from the study; (3) whether all participants met entry criteria; (4) whether continuation of the study is justified on the basis that additional data are needed to accomplish the stated aims of the study; and (5) conditions whereby the study might be terminated prematurely. The annual report will be signed by Dr. Lynn (ISM) and will be forwarded to the IRB and NIH/NINR. The IRB will review progress of this study on an annual basis.

SECTION D. Multi-Site Monitoring and Compliance
This is not a multi-site study.

SECTION E. Assessment of External Factors
The PI will conduct a semiannual assessment of external factors through a review of literature related to new developments in the areas of wound management, pain, exercise and other approaches that may have an impact on the safety of participants or on the ethics of the study.

SECTION F. Interim Analysis
The PM will generate semi-annual qualitative interim analysis reports on data obtained during phone call and returned end-of-study surveys to understand issues related to the uptake, usability, and adoption of this platform among this population. We will evaluate the screening and enrollment procedures, barriers to participation and retention, acceptability, technology problems encountered if any, and user feedback from the participants and providers. This information gained from this structured process will be used to both guide the refinement of the current protocol and to inform the design of a larger efficacy trial. There are no planned stopping rules for this study.

8.3.3.3 EXPECTEDNESS

N/A

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

See DSMP above for detail

8.3.5 ADVERSE EVENT REPORTING

See DSMP above for detail

8.3.6 SERIOUS ADVERSE EVENT REPORTING

See DSMP above for detail

8.3.7 REPORTING EVENTS TO PARTICIPANTS

See DSMP above for detail

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

If a woman becomes pregnant while she is in the study she will be withdrawn and follow-up ensured with her obstetric health care provider.

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

See DSMP above for detail

8.4.2 UNANTICIPATED PROBLEMS REPORTING

See DSMP above for detail

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Aim 1: Test the efficacy of the intervention in slowing adiposity and weight gain trajectory and improving health behaviors (nutrition and physical activity) in 4-year-old Hispanic children from Time 1 (0 months [baseline]) to Time 2 (9 months [completion of the intervention]) and Time 1 to Time 3 (15 months [after 6 months with no contact from the study staff]).

Aim 2: Test the efficacy of the intervention in decreasing adiposity and weight and improving health behaviors and self-efficacy in overweight or obese Hispanic mothers from Time 1 to Time 2 and from Time 1 to Time 3.

Primary outcomes include slowing of child adiposity (waist circumference and triceps and subscapular skinfolds) and weight gain (BMI percentile) trajectory and a decrease in mother's adiposity and weight (BMI). We hypothesize that intervention group children will slow the trajectory of adiposity and weight gain and intervention group mothers will decrease adiposity and weight significantly more than the control group.

Secondary outcomes include child and mothers health behaviors (nutrition and physical activity) and mother's self-efficacy (nutrition and physical activity). We hypothesize that intervention group children and mothers will improve health behaviors and mothers will improve self-efficacy significantly more than the control group.

Aim 3: Identify the mediators through which the intervention influences the trajectory of adiposity and weight gain in children and decrease in adiposity and weight in mothers. We hypothesize that health behaviors and self-efficacy may mediate adiposity and weight loss in mothers and nutrition and physical activity behaviors in children may mediate a slower adiposity and weight gain trajectory.

Aim 4: Calculate the cost of implementing the intervention for public health departments and the costs for mothers participating, from Time 1 to Time 2 and compare these costs to the outcomes of the intervention (cost-effectiveness) and the potential economic benefits of these outcomes (cost-benefit analysis). We hypothesize that the intervention is primarily focused on knowledge and behaviors in an at-risk population and may be cost-effective in comparison with other approaches to managing overweight and obesity.

Exploratory Aim: Determine whether intervention group mothers in the overweight versus obese BMI category benefit equally from the intervention in adiposity, weight, health behaviors, and self-efficacy.

9.2 SAMPLE SIZE DETERMINATION

A total of 250 mother-child dyads, or 125 dyads in each randomized group, are expected to complete the study. However, we will enroll 294 mother-child dyads (n = 588 participants) or 147 dyads per group, to take into account a 15% attrition rate. Our previous studies with Hispanic mothers with limited English proficiency and their children have had attrition rates ranging from 9% to 15% [23, 33]. Power calculations were performed with POWERLIB20 SAS/IML modules, which incorporate methods described in Muller [39]. These methods calculate power for a general linear multivariate model that includes repeated measures data structures, of which a two-group longitudinal design is a special case. Power was calculated on the use of a separate multivariate model for each outcome addressed in the aims, incorporating measurements at all available time points. Effect size estimates were based on the pilot data [23], where estimated within-subject correlation and standardized mean difference were .25 and .53, respectively, for mothers' BMI and .30 and .59, respectively, for children's BMI percentiles. For each outcome, power was computed for a test of the time by treatment interaction at a two-sided significance level of .05. For an analyzable sample of 125 mother-child dyads per group (total of 250 mother-child dyads), calculated statistical power exceeds 95% for both the test of children's BMI percentiles in Aim 1 and the test of mothers' BMI in Aim 2; if the within subject correlations and standardized mean differences are lower than observed in the pilot at .20 and .45, respectively, statistical power will nonetheless exceed 80%. A formal power analysis was not conducted for Aim 3 because the focus is on estimation (rather than testing) of direct and indirect mediation effects. Nonetheless, based on Shrout and Bolger [40], a sample size of 80 to 85 should provide power in the 70% to 85% range to detect medium effects of the intervention on the mediator (e.g., maternal self-efficacy), and the mediator on the outcomes (e.g.,

mother's BMI) with a two sided .05 significance level. Our 250 dyads should provide an adequate sample to quantify mediation of the relevant variables.

9.3 POPULATIONS FOR ANALYSES

Means, standard deviations, minimums, medians, and maximums will be determined for each continuous variable; frequencies and percentages will be tabulated for each categorical variable. Preliminary analyses will be performed to determine whether, despite randomization, the intervention and control groups were unbalanced on gender, age, or income. Any variable with an imbalance between the groups at baseline will be examined to determine whether it is related to any of the outcome variables. If significant relationships are identified, the variable will be included as a covariate in the models for the affected outcome(s) as a potential confounder. An intent-to-treat analysis will be used in which all subjects are included in the analysis and analyzed according to their initial randomized assignment.

9.4 STATISTICAL ANALYSES

Aim 1: To test the efficacy of the intervention in decreasing trajectory of adiposity and weight gain in 4-year-old children, separate mixed models will be used to test longitudinal differences between the intervention and control group means for each outcome across the study period. Mixed effects models, with a random intercept to account for between-mother or between-child differences, will be used for repeated measures analyses of each outcome (child BMI percentile, waist circumference, and triceps and subscapular skinfolds). The dependent variable will be will be the outcome at each of the three time points; the model will include time point (categorical), intervention group, and the interaction between the two. A test of this interaction will serve as the overall test of intervention effect, and step-down tests will be conducted to compare Time 2 and Time 3 to Time 1, and to estimate how or whether the intervention effect changed from Time 2 to Time 3, using a Hochberg correction to account for multiple comparisons [41, 42]. Results will be summarized through the least-squares means for each group at each time point and the mean difference and corresponding 95% confidence interval.

Aim 2: To test the efficacy of the intervention in decreasing adiposity and weight in mothers, we will fit mixed models analogous to those described for Aim 1 with each of the primary outcomes (mother's BMI and adiposity measures: waist circumference, and triceps and subscapular skinfolds) and secondary outcomes (child health behaviors: nutrition and physical activity, mother's health behaviors: nutrition and physical activity, and mother's self-efficacy: nutrition and physical activity).

Aim 3: To identify the mediators through which the intervention influences weight management in mother-child dyads, the approach of Shrout and Bolger [40] will be employed. This method, based on bootstrapping, builds on established mediation testing procedures, such as the Baron and Kenny approach [43] and the Sobel test [44]. Mediation analyses test pathways by which an explanatory variable (X) is theorized to influence the

mediator (M), which in turn influences the outcome (Y). Models will be conceptualized for each measure of weight and adiposity for mothers identified in Aim 1 (Y) and for each proposed mediator (M), relative to the randomized intervention group (X). For each model, an effect ratio (defined as the ratio of the indirect effect to the total effect, yielding the proportion of the effect that is mediated) and its bootstrapped distribution will be computed to assess the strength of mediation. Mediators (M) to be tested are improvements in health behaviors and self-efficacy. For example, we will analyze the effect of the intervention on change in maternal self-efficacy from baseline to Time 2, and, in turn the effects of this change in maternal self-efficacy at Time 2 on change in maternal BMI at Time 3.

Sensitivity analyses for Aims 1-3. Site will be included in all the models, and we will look for evidence of differential effects across cohort or site. The primary analyses use all available data, but if there is evidence of differential missingness by treatment group, we will use imputation methods as a sensitivity analysis.

Aim 4: We will calculate the incremental cost-effectiveness of the intervention, carried out from society's perspective as:

$$CE_{ij} = \frac{C_i - C_j}{E_i - E_j}$$

Where C is cost over the time period of the study; E is effectiveness measured by the outcomes; *i* refers to the intervention and *j* refers to the control group. We will calculate cost-effectiveness for the principal outcomes of the study; including cost per unit of BMI reduction, and cost per unit of improvement on the nutrition and physical activity self-efficacy scales. We will carefully track and calculate the costs of the program intervention activities and the control group activities, in order to measure the differences between the costs in the two groups. These costs will include hiring interventionists for all aspects of the Healthy Mothers-Healthy Children intervention. We will track the time invested in the program by participants in both the intervention and control group and calculate the value of time (opportunity cost) relative to the mothers' average income.

Exploratory Aim: Analyses will be performed on weight status, adiposity, health behavior, and self-efficacy to explore whether the intervention effects for mothers are similar for those who are overweight (BMI 25-29.9kg/m^2) and those who are obese (BMI $\geq$30 kg/m^2). The mixed models described for Aims 1 and 2 will be implemented for each of the weight status, adiposity, health behavior, and self-efficacy variables, with the addition of four explanatory variables to each model: an indicator for the obese group, the interaction between this indicator and the indicator variable for group membership, the interaction between this indicator and time, and the three-way interaction among the group indicator, obese indicator, and time. The hypothesis test for the three-way interaction as well as the obesity indicator by group indicator interaction jointly equal to zero will indicate whether the intervention effects are homogeneous across BMI ranges. For each outcome, differences will be calculated to test the effects of the intervention versus control group at each follow-up point separately for each BMI range. Similar analyses will be performed with groupings of children in the 25th-84.9th percentile (normal weight), 85th-94.9th percentile (overweight) and $\geq$95th percentile (obese).

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1.1 INFORMED CONSENT PROCESS
10.1.1.2 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS
10.1.1.3 CONSENT PROCEDURES AND DOCUMENTATION

See human subjects section above for details of consent.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

At the completion of five years or 60 months the study will be closed unless a no cost extension is needed.

10.1.3 CONFIDENTIALITY AND PRIVACY

See Human Subjects above.

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor or funding agency, representatives of the Institutional Review Board (IRB), regulatory agencies or representatives from companies or organizations supplying the product, may inspect all documents and records required to be maintained by the investigator for the participants in this study.

The study participant's contact information will be securely stored at the site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor/funding agency requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored on REDCap. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the University of North Carolina at Chapel Hill School of Nursing.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies
It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality
To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see *https://humansubjects.nih.gov/coc/index*). As set forth in 45 CFR Part

75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored at the University of North Carolina School of Nursing. After the study is completed, the de-identified, archived data will be transmitted to and stored at the University of North Carolina School of Nursing, for use by other researchers including those outside of the study.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	**Medical Monitor or Independent Safety Monitor**
Dr. Hudson Santos	Dr. Mary Lynn
The University of North Carolina at Chapel Hill	The University of North Carolina at Chapel Hill
Campus Box 7460	Campus Box 7460
919-259-4812	919-966-5450
hsantosj@email.unc.edu	Mary_Lynn@unc.edu

See DSMP Above

10.1.6 SAFETY OVERSIGHT

Safety oversight will be under the direction of a Data and Safety Monitoring Plan (DSMP) composed of individuals with the appropriate expertise. See the DSMP for details.

10.1.7 CLINICAL MONITORING

N/A

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Procedures will be followed according to standard protocols for height, weight, calculation of BMI and BMI percentile and collection of anthropometric measurements and questionnaire and accelerometry and 24 hour food recall data.

Quality control (QC) procedures will be implemented as follows:

Informed consent --- Study staff will review both the documentation of the consenting process as well as a percentage of the completed consent documents. This review will evaluate compliance with GCP, accuracy, and completeness. Feedback will be provided to the study team to ensure proper consenting procedures are followed.

Source documents and the electronic data --- Data will be initially captured on source documents and will ultimately be entered into the study database. To ensure accuracy site staff will compare a representative sample of source data against the database, targeting key data points in that review.

Intervention Fidelity — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described above.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection will be the responsibility of the Principal Investigator at the site under the supervision of the Project Manager. The investigator will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents will be completed in a neat, legible manner to ensure accurate interpretation of data.

Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each participant consented/enrolled in the study. Data recorded in the electronic case report form (eCRF) derived from source documents will be consistent with the data recorded on the source documents.

Clinical data will be entered into REDCap, a 21 CFR Part 11-compliant data capture system provided by the University of North Carolina at Chapel Hill. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

10.1.9.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 5 years.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers 5 years after the completion of the primary endpoint by contacting the Principal Investigator.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the NINR has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
CFR	Code of Federal Regulations
COC	Certificate of Confidentiality

CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FFR	Federal Financial Report
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICH	International Council on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ITT	Intention-To-Treat
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale
2	2019-06-19	Updated to include 3-5 year old children	Increase sample

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