TEEN HEED Protocol

Protocol Number*: <1>

National Clinical Trial (NCT) Identified Number: <Number, once assigned by CT.gov>

Principal Investigator*: Nita Vangeepuram, MD, MPH

Sponsor: Icahn School of Medicine at Mount Sinai

Grant Title: TEEN HEED

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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 Acceptance of this document constitutes agreement by the recipient that no unpublished information contained herein will be published or disclosed without prior approval of the Principal Investigator or other participating study leadership and as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, as described in the *Statement of Compliance* above.

Principal Investigator or Clinical Site Investigator:

Signed: _____ Date: _____

Name*:

Title*:

Investigator Contact Information

Affiliation*:

Address:

Telephone:

Email:

[For multi-site studies, the protocol should be signed by the clinical site investigator who is responsible for the day to day study implementation at his/her specific clinical site.]

Signed: _____ Date: _____

Name:

Title:

Affiliation:

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: TEEN HEED: An Adolescent Peer Led Diabetes Prevention Intervention

Grant Number: <Grant Number>

Study Description: Specific Aims: 1) Explore strategies for using peer educators and novel mobile health technologies as part of a group lifestyle change program for diabetes prevention among at-risk ethnic minority youth in a New York City community with high disease burden. 2) Refine, implement, and evaluate outcomes for the intervention. Using preliminary data, we will use CBPR to refine our developmentally and culturally appropriate lifestyle intervention for pre-diabetic ethnic minority adolescents. We will then screen at-risk adolescents for pre-diabetes and related lifestyle and biological measures and compare outcomes in adolescents in intervention and wait list control groups to test intervention effectiveness. 3) Further refine the intervention for a larger RCT based on an examination of intervention feasibility, acceptability, and sustainability.

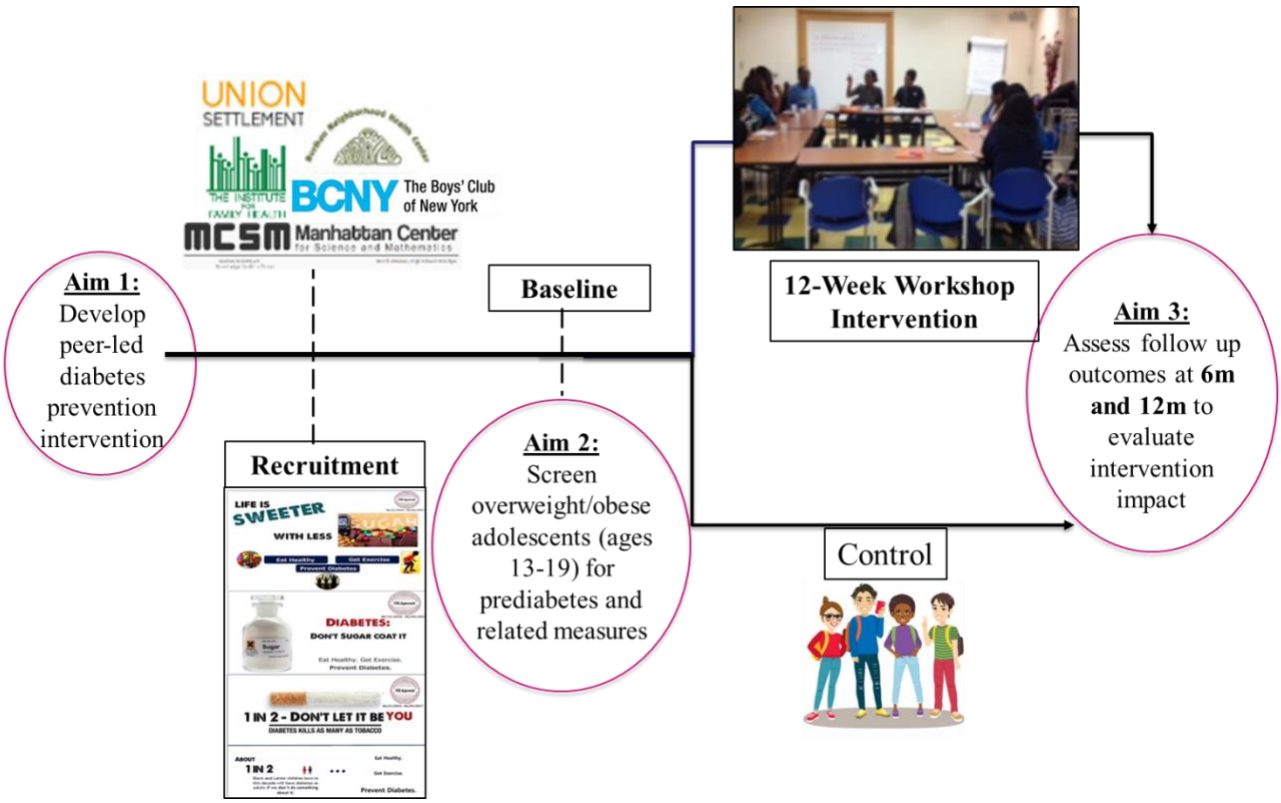
Objectives*: The specific aims of the TEEN HEED (Help Educate to Eliminate Diabetes) Trial are to:

1. Use an iterative process between academic and community partners to adapt and modify the pilot TEEN HEED intervention
2. Use qualitative methods to evaluate strategies for using peer educators and novel mobile health technologies as part of a group lifestyle change program for diabetes prevention among at-risk ethnic minority youth
3. Use community-based participatory research strategies to refine, test, and evaluate outcomes of a peer education diabetes prevention program for pre-diabetic ethnic minority adolescents.
4. Examine intervention feasibility, acceptability, and sustainability.

Endpoints*:	**Evaluation of the intervention's impact on the primary study outcome, participants' weights:** We hypothesize that the TEEN HEED intervention will result in maintenance or decrease in BMI percentile. Evaluation of the effectiveness of the TEEN HEED intervention on behaviors and mediators related to weight loss and diabetes prevention: We hypothesize that the intervention will lead to observable changes to diet, physical activity and weight control behaviors and that these and other mediators explain weight loss.
Study Population:	*This study involves adolescents ages 13-19.*
Phase* or Stage:	*N/A*
Description of Sites/Facilities Enrolling Participants:	*All programming will be offered via Zoom. In-person study visits for baseline, 5m, and 12m, will be conducted at our pediatric clinic.*
Description of Study Intervention/Experimental Manipulation:	*12 week virtual workshop (offered via zoom) that covers behavioral skills including goal setting, self-monitoring, problem solving, contingency management, coping skills, and social support. Workshop topics included explanation of pre-diabetes/diabetes, label reading, healthy plate planning, portion control, finding affordable healthy foods, strategies to increase physical activity, and coping with eating triggers and social pressures. Participants create and report on action plans with weekly goals, brainstorm to solve problems, and communicate between sessions.*
Study Duration*:	*3 years*
Participant Duration:	*12m*

1.2 SCHEMA

Flow Diagram *(e.g., randomized controlled trial)*



1.3 SCHEDULE OF ACTIVITIES (VIRTUAL TEEN HEED)

	Pre-screening (Pre-consent)	Visit 1 Baseline	12-week workshop	3m visit
EMR Review Eligibility	X			
Informed Consent		X		
Demographics		X		
Clinical history		X		
Height & Weight		X		X
Outcome Evaluation				
Workshop assessments/Action Planning			X	
Health and Lifestyle Questionnaire		X		X
Debrief session			X	
Adverse Events Reporting		X	X	X

2 INTRODUCTION

2.1 STUDY RATIONALE

The number of youth with type 2 diabetes in the U.S. is projected to increase by 49 percent by 2050, with higher rates among minority youth. The Diabetes Prevention Program (DPP) is recognized as a sentinel study demonstrating the effectiveness of lifestyle interventions for diabetes prevention among pre-diabetic adults but has not yet been replicated in youth. In addition, such intensive interventions are often not sustainable in high risk communities with limited resources. One strategy that has been successfully employed in adults from such communities is peer based health education. Research suggests that like adults, young people are more likely to hear and personalize messages, and thus to change their attitudes and behaviors, if they believe the messenger is similar to them and faces the same concerns and pressures. However, there have been no peer led interventions in ethnic minority teens and no interventions focused specifically on weight loss for diabetes prevention. Finally, another challenge identified in existing youth health intervention programs is keeping youth engaged to enhance program participation and impact. One potential strategy is the use of mobile technologies (text messaging, mobile applications, social media) to support weight management programs, but to date use of such technologies has not been studied in youth. This study's overall objective is to use community-based participatory research (CBPR) to develop and pilot test a youth peer-led diabetes prevention intervention incorporating novel mobile health technologies for at-risk adolescents in a vulnerable New York City community. The central hypothesis is that such an intervention will lead to maintenance or decrease in BMI, improved dietary, physical activity and weight control behaviors, and decrease in diabetes risk.

2.2 BACKGROUND

Our Previous Study: People who develop diabetes go through a period when they have "pre-diabetes," defined by the American Diabetes Association as fasting blood glucose of 100-125 mg/dl, and/or 2-hour post-prandial blood glucose of 140-199 mg/dl, and/or hemoglobin A1c of 5.7-6.4%. Diabetes and pre-diabetes are being diagnosed more in children, likely related to increasing rates of obesity. National estimates are that about 16% of all adolescents have pre-diabetes with higher rates in obese adolescents or those with a family history of diabetes.

Weight loss is the single therapy proven to prevent diabetes. In clinical settings, overweight adults with pre-diabetes who reduce their weight by 5-10% can reduce their risk of developing diabetes by 55-60%. While there have been no large diabetes prevention trials in children and adolescents, school based, clinic-based and community-based trials have led to reduction in diabetes risk (improvements in body measurements and glucose or insulin levels) with intensive lifestyle interventions.

An effective low-resource diabetes prevention strategy devised for adults in high-risk communities is the use of peer leaders to promote lifestyle change. Investigators from the adult HEED study (GCO#05-0463) conducted a randomized-controlled trial to compare the effectiveness of peer-led community-based workshops, versus usual care (delayed intervention) in achieving weight

loss and prevention of diabetes among overweight (BMI > 25) adults with pre-diabetes in East Harlem. Over 400 adults with pre-diabetes were identified through the standard protocol for pre-diabetes screening, an oral glucose tolerance test (OGTT) (a fingerstick test with an instant read glucose analyzer). The OGTT is performed by measurement of glucose, both at fasting and after administration of a 75 gram oral glucose load. Adults with pre-diabetes were randomized to intervention and delayed intervention groups to test the effectiveness of the HEED intervention. Pre-diabetics in the intervention group had statistically significant weight loss maintained at one year and a leveling of their glucoses, as compared with controls.

Research suggests that like adults, young people are more likely to hear and personalize messages, and thus to change their attitudes and behaviors, if they believe the messenger is similar to them and faces the same concerns and pressures. However, relatively few studies have focused on peer led lifestyle interventions in youth. In the first pilot phase of the TEEN HEED intervention (GCO # 11-1711), we adapted the HEED intervention for East Harlem adolescents. We conducted community based screening for pre-diabetes among 56 at-risk obese adolescents. We measured glucoses using oral glucose tolerance tests. Adolescents completed a survey to assess diet and physical activity knowledge, attitudes and behaviors and diabetes risk. They also underwent detailed body measurements (i.e. height, weight, body fat, waist circumference) and blood pressure testing.

Nineteen adolescents diagnosed with pre-diabetes had more detailed assessment of their dietary intake and physical activity levels. Pre-diabetic adolescents were then invited to take part in an initial version of the TEEN HEED intervention. Trained adolescent peer educators partnered with experienced adult HEED workshop leaders to run the workshops. At follow up, participants again completed the oral glucose tolerance test, verbally administered questionnaire, body measurements (i.e. height, weight, body fat, waist circumference) and blood pressure testing. Out of 9 adolescents who completed at least 4 out of 8 workshop sessions led by trained teens, 5 had decreased BMI and 5 no longer had pre-diabetes at 3 month follow up.

To supplement what we have learned through the pilot study, we completed additional qualitative studies to further develop our intervention. We conducted focus groups to explore 1) peer influences on eating behaviors, physical activity, and other individual factors related to weight management, 2) strategies for further adapting our peer education diabetes prevention intervention for urban minority adolescents, and 3) use of mobile technologies (such as text messaging, mobile applications and social media) as an adjunct to the peer-led intervention.

We then recruited participants ages 13-19 who are at risk for diabetes through community youth organizations, health centers and schools, determined eligibility (overweight/obese by measured BMI), and invited them to return fasting for further evaluation. Those ages 13-17 required assent/parental consent, while those $\geq$18 signed their own consent. We screened teens for pre-diabetes using an oral glucose tolerance test (OGTT),[59] obtained body measurements, blood pressure and metabolic tests, and administered a health and lifestyle survey. We screened 148 teens, of whom 90 were diagnosed with pre-diabetes (61%) and were randomized to intervention (n=41) and wait list control (n=49) groups. Each workshop group (10-15 teens) met for 90 minutes weekly for 12 weeks. All activities were delivered under the supervision of experienced adult health educators by youth peer leaders who underwent training including team building, group facilitation, and review of the workshop curriculum. We collected 5 and 12

month follow up data (73% retention at both time points). Information from this previous cohort will be used to refine our study.

In order to maximize the reach of this intervention, and with increasing need due to the pandemic, we are proposing a virtual component to the TEEN HEED program.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

The loss of information always exists, however provisions have been made to mitigate these risks. Participants may feel uncomfortable with the survey questions, or being in a group setting. We discuss this with participants at all times to measure their comfort and mitigate any concerns. Participants are also able to skip questions with which they are particularly uncomfortable.

2.3.2 KNOWN POTENTIAL BENEFITS

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS
Primary	
Use an iterative process between academic and community partners to adapt and modify the pilot TEEN HEED intervention Use qualitative methods to evaluate strategies for using peer educators and novel mobile health technologies as part of a group lifestyle change program for diabetes prevention among at-risk ethnic minority youth Use community-based participatory research strategies to refine, test, and evaluate outcomes of a peer education diabetes prevention program for pre-diabetic ethnic minority adolescents.	1) maintain/reduce body mass index (BMI) 2) improve adolescent dietary, physical activity and weight control behaviors, and 3) improve other measures of diabetes risk. We are collecting data at baseline and post intervention. We are also obtaining additional qualitative data and examining feasibility and acceptability for a text messaging program to support teens as they make lifestyle changes.

4 STUDY DESIGN

4.1 OVERALL DESIGN

We are now testing and evaluating outcomes of our refined intervention to reduce diabetes risk among ethnic minority pre-diabetic adolescents. We will further adapt the program for virtual delivery via a video conferencing platform to enhance access and attendance, and refine the text messaging platform to better support and engage teens.

We will identify at risk for diabetes adolescents and recruit adolescents (BMI in the overweight/obese range and HbA1c 5.7-6.4%) through electronic medical record data queries and referrals from clinical and community sites. Participation will be contingent on adolescent assent/parental consent (ages 13-17) or participant consent (ages 18 years or older). We will randomize pre-diabetic adolescents into intervention and wait list control (delayed intervention) groups to test intervention effectiveness. We will also evaluate the virtual and mHealth components of the intervention through usability testing and data analytics.

The intervention is 12 weekly 90-minute workshops based on feedback from our community advisory board and experts in peer led health education programs. The intervention will be offered via an online platform, Zoom, which is HIPAA compliant. We are testing the effectiveness of a virtual component versus our previous in-person workshop.

We are currently developing a technology-based component of the intervention based on findings from focus groups and with input from our Community Advisory Board (CAB). The technology-based tool is a secure mobile health platform we are developing in collaboration with a company called mPulse Mobile. The platform will allow us to securely send and track text messages, help participants set goals and monitor their behaviors, and provide participants with individualized feedback and positive reinforcement. Messages will be sent via an SMS text messaging mobile health platform to provide motivational messages regarding healthy eating, physical activity and healthy weight maintenance and to follow up on weekly goals made by the participants. The platform supports interactive dialogues including automated interactions using rule-based branching logic that allows participants to navigate through the program based on their message responses. In addition, natural language understanding allows real-time interpretation of text responses for more sophisticated dialogues. Beyond processing responses through automated dialogues, natural language understanding allows for responses that fall outside the scope of the dialogue's rules. mPulse Mobile's Engagement Console allows project staff to manage individual interactions with participants. The Console identifies any responses that cannot be handled by the messaging program's rules and flags these messages for staff to resolve. Additionally, staff can use the Console to manually initiate messages, and high-priority messages that must be reviewed can be escalated in real-time.

All information within the mPulse Mobile platform and cloud server is protected and secure. The platform ensures privacy and confidentiality of information shared and messages sent. The HITRUST Common Security Framework (CSF) is the most widely-accepted information technology security control audit framework developed explicitly for the protection of healthcare information. The framework integrates requirements from sources such as ISO, NIST, PCI, HIPAA, and others. To successfully complete the HITRUST CSF audit, mPulse Mobile had to

undergo a rigorous third-party vetting process consisting of baseline controls across many domains including information protection, endpoint protection, configuration management, disaster recovery, risk management, and physical security.

mPulse Mobile messaging programs follow compliance principles guided by Telephone Consumer Protection Act, Mobile Marketing Association's Consumer Best Practices, and CTIA Mobile Compliance Assurance Handbook. Dr. Nita Vangeepuram will be the application manager.

All participants will also be advised about privacy issues surrounding responses to text messages. It will be recommended that they use a password to protect their cell phones. (Please see the previously submitted IT Security Risk Assessment Report).

We will be piloting the texting program with participants who had previously been enrolled in earlier version of the TEEN HEED study. We will obtain parental permission to allow mPulse Mobile to receive their cell phone numbers and send SMS text messages to participants. This information will be included in the study consent form with a separate place within the consent form for parents to initial to give this permission. Participants aged 18-19 will be asked to sign their own permission to receive SMS text messages from mPulse Mobile. We will make it very clear to participants that what is shared through the mobile dialogue is private, secure, and not shared with anyone beyond the program. We will also express that standard data and messaging rates from participant's provider may apply and that they can request that messages stop being sent at any time.

We will also conduct audio-recorded debriefing sessions with participants and peer leaders in which we will ask about their experiences with the intervention, reactions to the intervention, and ideas for intervention refinement. To monitor the community-academic partnership, we are tracking activities such as the communication between community-academic partners, number of participants at CAB meetings, number of manuscripts and presentations by academic-community partners, and policy-related outcomes. Additionally, we are investigating youth involvement in CBPR, through audio-recorded one-on-one interviews and qualitative analysis. This will help us understand how young people have helped shape the project. We are interviewing study participants, peer leaders, community action board members, interns, and study coordinators. They are being consented and asked questions about their personal experience with the study and their views on how young people have contributed to the project and how they may continue to do so in the future.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

Research suggests that like adults, young people are more likely to hear and personalize messages, and thus to change their attitudes and behaviors, if they believe the messenger is similar to them and faces the same concerns and pressures. However, relatively few studies have focused on peer led lifestyle interventions in youth.

4.3 JUSTIFICATION FOR INTERVENTION

Rates of new diagnosed cases of type 2 diabetes are increasing among youth in the United States, with a disproportionate increase among minority youth. Lifestyle interventions leading to weight loss have

proven to be effective for diabetes prevention among overweight prediabetic adults, but few have been developed and tested in youth.

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed the baseline assessment and the follow-up assessment or has completed the text messaging program.

The end of the study is defined as completion of the 3-month follow-up assessment shown in the Schedule of Activities (SoA), **Section 1.3**.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

INCLUSION CRITERIA:

- Adolescents ages 13-19 years of age
- Residents of East or Central Harlem, members of an East or Central Harlem Institution, or patients seen in the Mount Sinai Health System. Membership in an East or Central Harlem institution includes the following: 1) attending a school in East or Central Harlem, 2) attending an after school or recreational activity in East or Central Harlem, or 3) receiving health care in East or Central Harlem. We will not ask participants for any identification for proof of address or membership in an East or Central Harlem institution. After informed consent is obtained for the adolescent to take part in the study, we will ask for the adolescent's full residential address. We will include those participants who live in supportive housing (such as shelters) and do not have plans to relocate from N.Y.C in the next year.
- Body mass index (BMI) percentile consistent with overweight/obesity (>85th percentile for age and gender based on Centers for Disease Control and Prevention definition).
- Hemoglobin A1c in prediabetes range (>5.7% or <6.5%)
- English speaking (resources available to us at this time limit inclusion of English speaking participants only). Note: only adolescents must be English speaking. Parental consent forms will be available in English and Spanish. The Spanish consent form will be submitted for IRB review with a letter of attestation from the translator after approval of the English consent form.
- Able to communicate verbally to participate in a group education class.
- Demographics:

(a) Gender:	Males	yes☒	no☐
	Females	yes☒	no☐

(b) Age range: from 13 to 19

(c) Racial and Ethnic Groups:

Caucasian	yes☒	no☐
Black	yes☒	no☐
Hispanic	yes☒	no☐
American Indian	yes☒	no☐
Alaskan Native	yes☒	no☐
Asian/Pacific Islander	yes☒	no☐

Other (specify) _____

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

- <13 or >19 years of age
- Previous diagnosis of diabetes
- BMI percentile <85th percentile for age and gender based on Centers for Disease Control and Prevention definition
- Hemoglobin A1c outside of the prediabetes range (<5.7% or >6.4%)
- Currently pregnant
- Speaking a language other than English (resources to translate and implement all study activities in other languages are limited at this time)
- Cognitive or physical impairment that would preclude comprehension of a conversation and communicating as part of a group (i.e., dementia, deafness, inability to speak)
- On medications that may raise or lower blood sugar
- Plans to relocate from New York City within one year of enrollment
- Had, or is planning to have gastric bypass surgery
- Has a pacemaker or other implanted electronic device

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in this study but are not subsequently assigned to the study intervention or entered in the study. Individuals who do not meet the criteria for participation in this trial (screen failure) because of meeting one or more exclusion criteria that are likely to change over time may be rescreened. Examples include the successful treatment of a previous affective disorder, and the lifting of physical activity restrictions previously in place. Rescreened participants will be assigned the same participant number as for the initial screening.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

The Principal Investigator Dr. Vangeepuram, Research Coordinator Ms. Elaiho and community partners working on this study previously identified venues for recruitment of adolescents in East

and Central Harlem including youth community based organizations, after school programs, and health care centers.

Recruitment sites may include the following community organizations in East Harlem with whom we have previously collaborated: Union Settlement Association, Harlem RBI, East Harlem Boys Club, Children's Aid Society, Stanley Isaacs Neighborhood Center, SCAN(SUPPORTIVE CHILDREN'S ADVOCACY NETWORK), Harlem Children's Zone, and other interested organizations to be identified by our community partners and project board. Possible clinical sites for recruitment include Mount Sinai's Adolescent Health Center, Mount Sinai's pediatric endocrine clinic, Mount Sinai's Pediatrics Associates practice, Settlement Health, Boriken Neighborhood Health Center, the Institute for Family Health, Mount Sinai School Based Health Clinics, and Mount Sinai Pediatric Emergency Rooms.

We will obtain provider referrals from community based clinics. We will use Mount Sinai's Data Warehouse and/or EPICs slicer/dicer to identify potentially eligible subjects for recruitment from the Mount Sinai General Pediatric Faculty Practice, Pediatric Endocrinology and Diabetes Center, and the School Based Health Clinics. We will request the following fields:

Name, medical record number, date of birth/age, address. gender, parent or guardian name, contact information for teens 18-19 (including telephone number or other numbers provided), parent or guardian contact information for teens ages 13-17 (including telephone number or other numbers provided), BMI (BMI percentile when available), medications prescribed, and laboratory values from the past year: Glucose/preserved glucose, hemoglobin A1c (values), total insulin (values), and lipid panels (values).We will request information for eligible patients whose medical records contain the following diagnoses codes: overweight, obesity, prediabetes, insulin resistance, and acquired acanthosis nigricans.

We will obtain only the minimum amount of PHI necessary to contact potentially eligible teenagers. We will meet with providers and ask them to consent to contacting their patients who they think may be eligible. Contact information will be immediately deleted from the server for those who are not interested in participating or who are not eligible for the study. Participants will be given the opportunity to decline being re-contacted should they not be interested in participating.

For Collaborating Community sites – As described above, site leaders will verbally inform potential subjects about TEEN HEED and provide interested children with a letter for parents. For adolescents ages 18 or 19 years who meet eligibility requirements and are interested in the study, we will obtain informed consent prior to participation in the study. For adolescents ages 13-17 years, who meet eligibility requirements and are interested in the study, we will obtain assent of the adolescent and obtain consent from his/her parent or guardian. The combined Parental Consent and HIPAA Authorization Form will be obtained in person or over the phone by a member of the study staff. After consent is obtained, we will invite adolescents for their official baseline visit. Eligible adolescents will be randomized into intervention and wait list control groups. Intervention participants will attend a 12-week peer led workshop and follow up assessments.

We will recruit potential peer leaders through our contacts at community youth organizations in East and Central Harlem and local schools. Peer leaders will attend training sessions, workshop

sessions and debriefing sessions. All classes will be led by trained adolescent peer leaders. Qualifications to be a peer leader are: 1) older than 18 years of age 2) fluency in English and 3) ability to communicate well in a group setting. Peer leader training will include information about not divulging information (e.g., conditions, treatments, personal background or any other confidential or non-public information) concerning participants attending the classes. We will also have the leaders sign a Statement of Confidentiality. Peer leaders will be paid $100 to attend the training session and $300 for leading each 12 week workshop

Participants will be given a $40 gift card at each study visit as compensation for their time.

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

Teen-led workshops cover behavioral skills including goal setting, self-monitoring, problem solving, contingency management, coping skills, and social support. Workshop topics include explanation of pre-diabetes/diabetes, label reading, healthy plate planning, portion control, finding affordable healthy foods, strategies to increase physical activity, and coping with eating triggers and social pressures. Participants create and report on action plans with weekly goals, brainstorm to solve problems, and communicate between sessions. The intervention is 12 weekly 90-minute workshops based on feedback from our community advisory board and experts in peer led health education programs. The intervention will be offered via an online platform, Zoom, which is HIPAA compliant. We are testing the effectiveness of the virtual program.

For participants in the text message pilot program we will obtain parental permission to allow mPulse Mobile to receive their cell phone numbers and send SMS text messages to participants. This information will be included in the study consent form with a separate place within the consent form for parents to initial to give this permission. Participants aged 18-19 will be asked to sign their own permission to receive SMS text messages from mPulse Mobile. We will make it very clear to participants that what is shared through the mobile dialogue is private, secure, and not shared with anyone beyond the program. We will also express that standard data and messaging rates from participant's provider may apply and that they can request that messages stop being sent at any time. Participants in the waitlist control will also be asked to consent to giving their phone numbers to mPulse

6.1.2 ADMINISTRATION AND/OR DOSING

Full-Dose: Attendance to all 12 workshops

Half-dose: Attendance to 6-11 workshops

Participants attending less than 4 workshops will be considered as "not adhering to the project"; however, they will not be removed from the study.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

The principal investigator and clinical research coordinator will be responsible for screening potential peer leaders to ensure that they are appropriate for being in a leadership position with younger teens. Potential peer leaders will likely be referred by staff at our collaborating youth organizations who have been working with these youth for years. Interested youth will complete applications. We will conduct thorough interviews and also contact adult references provided as part of the leader selection process. Youth peer leaders will receive training about the workshops and communication/leadership skills and will be supervised by experienced adults throughout the study.

All members of the study team will be adequately trained on the protocol through planning meetings prior to the launch of this study. New study members will be trained through the use of scripts and a training manual developed for all trial-related functions. This training manual includes detailed instructions for each recruitment event, including participant checklists, device protocols, and results explanations. Research staff will use the scripts provided in the training manual for all study events. Debriefing will occur after each recruitment and follow-up event to confirm procedures and adherence to protocol.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

We are not randomizing participants for this pilot study.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

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

When a subject discontinues from the study intervention (12-week workshop) but not from the study, remaining study procedures will be completed as indicated by the study protocol. If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed.

The data to be collected at the time of study intervention discontinuation will include the following:

- The reason(s) for discontinuing the participant from the intervention, and methods for determining the need to discontinue
- If the participant is due to complete assessments within 2 weeks of being discontinued from the study intervention, those assessments will be administered at the time of discontinuation; if the next scheduled assessments are more than 2 weeks from the discontinuation date, the discontinued participant will wait for the next scheduled assessment. Thereafter, the participant will be included in all future scheduled assessments, even though not participating in the intervention.

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 the following reasons:

- Significant study intervention non-compliance, unless varying compliance is an aspect of the study objectives
- Lost-to-follow up; unable to contact subject (see **Section 7.3, Lost to Follow-Up**)
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

Subjects who sign the informed consent form, 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 he or she fails to return for the follow up visit scheduled visit 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 to the clinic for a required study visit:

- The site will attempt to contact the participant, reschedule the missed visit within 1 month, 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, emails and text messages and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). 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

Evaluation of the intervention's impact on the primary study outcome, participants' weights: We hypothesize that the TEEN HEED intervention will result in maintenance or decrease in BMI percentile. We chose this outcome because weight loss is consistently shown as the most powerful and effective diabetes prevention strategy.

Evaluation of the effectiveness of the TEEN HEED intervention on behaviors and mediators related to weight loss and diabetes prevention: We hypothesize that the intervention will lead to observable changes to diet, physical activity and weight control behaviors and that these and other mediators explain weight loss. We will assess whether the intervention leads to improvements in diet and physical activity behaviors and related mediators such as knowledge, attitudes, beliefs, self-efficacy, and social influences, and improvements in other measures of diabetes risk (such as HbA1c). Hypotheses will be tested by comparing changes in outcomes between baseline post-intervention follow-up. We will also conduct exploratory analyses to begin to understand whether any of these factors appear closely linked to pre-diabetes diagnosis or weight loss.

8.2 SAFETY ASSESSMENTS

We will adhere to the minimum DSMP standards of the PPHS as this study does not involve more than minimal risk to subjects.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS

This protocol uses the definition of adverse event from 21 CFR 312.32 (a): any untoward medical occurrence associated with the use of an intervention in humans, ***whether or not considered intervention-related***.

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.

- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".]

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All adverse events (AEs) will have their relationship to study procedures, including the intervention, assessed by an appropriately-trained clinician based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Related** – The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.
- **Not Related** – There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

8.3.3.3 EXPECTEDNESS

A clinician with appropriate expertise in pre-diabetes will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study procedures.

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

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor.

All AEs, not otherwise precluded per the protocol, will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study procedures (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study will be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical or psychiatric condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. Documentation of onset and duration of each episode will be maintained for AEs characterized as intermittent.

<Insert role or name> will record events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

8.3.5 ADVERSE EVENT REPORTING

8.3.6 SERIOUS ADVERSE EVENT REPORTING

N/A

8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

8.3.8 EVENTS OF SPECIAL INTEREST

N/A

8.3.9 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the Data Coordinating Center (DCC)/lead principal investigator (PI). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to the IRB and to the DCC/study sponsor/funding agency within <insert timeline in accordance with policy> of the investigator becoming aware of the event
- Any other UP will be reported to the IRB and to the DCC/study sponsor/funding agency within <insert timeline in accordance with policy> of the investigator becoming aware of the problem
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) within <insert timeline in accordance with policy> of the IRB's receipt of the report of the problem from the investigator

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Evaluation of the intervention's impact on the primary study outcome, participants' weights: We hypothesize that the TEEN HEED intervention will result in maintenance or decrease in BMI percentile. We chose this outcome because weight loss is consistently shown as the most powerful and effective diabetes prevention strategy.

Evaluation of the effectiveness of the TEEN HEED intervention on behaviors and mediators related to weight loss and diabetes prevention: We hypothesize that the intervention will lead to observable changes to diet, physical activity and weight control behaviors and that these and other mediators explain weight loss. We will assess whether the intervention leads to improvements in diet and physical activity behaviors and related mediators such as knowledge, attitudes, beliefs, self-efficacy, and social influences, and improvements in other measures of diabetes risk (such as HbA1c). Hypotheses will be tested by comparing changes in outcomes between baseline and post-intervention follow-up. We will also conduct

exploratory analyses to begin to understand whether any of these factors appear closely linked to pre-diabetes diagnosis or weight loss.

9.2 SAMPLE SIZE DETERMINATION

9.3 POPULATIONS FOR ANALYSES

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

We will use descriptive statistics to summarize the variables. Analyses will primarily test the hypothesis that intervention participants will have maintenance/reduction of BMI. Secondary analyses will assess whether the intervention leads to improvements in diet and physical activity behaviors and related mediators such as knowledge, attitudes, beliefs, self-efficacy, and social influences. Hypotheses will be tested by comparing changes in outcomes between baseline and follow up. Initial bivariate comparisons will use t tests to compare continuous endpoints and the Wilcoxon matched pairs signed-rank test to compare ordinal endpoints. We will then conduct multivariable analyses (using logistic regression, general linear models, and mixed models) to adjust for potential confounders (such as age, race/ethnicity, gender, SES, and baseline BMI) and to account for the repeated observations per participant. Analyses will include the baseline level of each endpoint as a covariate and a continuous variable for time. Confidence intervals will be constructed around each parameter estimate of the intervention. We will estimate effect sizes for each measure using correction for small sample bias.

To monitor the community-academic partnership, we will track activities such as the communication between community-academic partners, number of participants at CAB meetings, number of manuscripts and presentations by academic-community partners, and policy-related outcomes. We will also ask CAB members to complete annual surveys to gauge how closely the research project aligns with principles of CBPR, including factors they may feel less comfortable discussing in a group, such as level of inclusion and trust.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

9.4.4 SAFETY ANALYSES

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Demographics: Age, Sex, BMI, Height, Weight, Waist Circumference, etc.

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

Evaluation of the intervention's impact on the primary study outcome, participants' weights: We hypothesize that the TEEN HEED intervention will result in maintenance or decrease in BMI percentile. We chose this outcome because weight loss is consistently shown as the most powerful and effective diabetes prevention strategy.

Evaluation of the effectiveness of the TEEN HEED intervention on behaviors and mediators related to weight loss and diabetes prevention: We hypothesize that the intervention will lead to observable changes to diet, physical activity and weight control behaviors and that these and other mediators explain weight loss. We will assess whether the intervention leads to improvements in diet and physical activity behaviors and related mediators such as knowledge, attitudes, beliefs, self-efficacy, and social influences, and improvements in other measures of diabetes risk (such as HbA1c). Hypotheses will be tested by comparing changes in outcomes between baseline and post-intervention follow-up. We will also conduct exploratory analyses to begin to understand whether any of these factors appear closely linked to pre-diabetes diagnosis or weight loss.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

- We aim to Recruit and enroll adolescents from clinical and community sites starting in the Spring 2021. Provisions may be made depending on the novel coronavirus pandemic.

9.4.9 EXPLORATORY ANALYSES

We hypothesize that the intervention will lead to observable changes to diet, physical activity, and weight control behaviors and that these, and other, mediators explain weight loss. We will also conduct exploratory analyses to begin to understand whether any of these factors appear closely linked to pre-diabetes

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

The study team will follow "SOP HRP -090 Informed Consent". Consent forms describing in detail the study intervention, study procedures, and risks will be given to the participant and written documentation of informed consent will be completed prior to starting the study intervention. The following consent materials are submitted with this protocol adult consent and parental consent in both English and Spanish.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

After participants are determined to be eligible for our study we will obtain informed consent over the phone, through REDCap, or in person. Due to the nature of the ongoing pandemic and many individuals limiting their exposure, multiple methods of obtaining consent are necessary.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to <study participants, investigator, funding agency, and regulatory authorities>. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance of study staff to the protocol (ie, significant protocol violations)
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB, Food and Drug Administration (FDA), or other relevant regulatory or oversight bodies (OHRP, DSMB).

10.1.3 CONFIDENTIALITY AND PRIVACY

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, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical 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.

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 Icahn School of Medicine at Mount Sinai. After the study is completed, the data will be stored for the recommended time of seven years after study completion. No samples or data will be stored for future use outside of the research designated by this protocol.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator	**Medical Monitor or Independent Safety Monitor**
Nita Vangeepuram, MD, MPH, Associate Professor	*Name, degree, title*
Icahn School of Medicine at Mount SInai	*Institution Name*
1 Gustave L. Levy Place Box 1198	*Address*
917.478.2106	*Phone Number*
Nita.vangeepuram@mssm.edu	*Email*

Nita Vangeepuram, MD, MPH is an Assistant Professor of Pediatrics, Preventive Medicine and Population Health Science and Policy at the Icahn School of Medicine at Mount Sinai (ISMMS) and a practicing general pediatrician. Dr. Vangeepuram's clinical, research and programmatic experience will help her develop the proposed adolescent diabetes prevention intervention. Dr. Vangeepuram helped to develop a pediatric weight management program (Junior Urban Movement Program, JUMP) at ISMMS. She received a grant from the American Academy of Pediatrics Community Pediatrics Training Initiative for Obesity Prevention to implement provider, community and advocacy initiatives related to pediatric obesity. Prior research work includes study of associations between obesity, diet, physical activity, neighborhood factors and asthma, as well as examination of disparities in diet and physical activity behaviors in children from different ethnic minority subgroups. Dr. Vangeepuram was a co-investigator in the East Harlem Diabetes Center of Excellence, and has experience conducting in depth interviews of community youth leaders and focus groups with East Harlem adolescents. She then obtained funding from an Empire Clinical Investigator Research Program grant and Mount Sinai's CTSA, which provided protected research time and support for the early pilot phase of the project. She was awarded an NIH Mentored Patient-Oriented Research Career Development Award (K23), and currently has R03 funding from NIH and funding from CIGNA Foundation which provide protected research time and project funding. She is the Engagement Core Lead for the Institute for Health Equity Research.

Carol R. Horowitz, MD, MPH, is Professor of Population Health Science and Policy and Medicine at Mount Sinai, and a practicing general internist. With a focus on using Community-Based Participatory Research to address health disparities, she has been the Principal Investigator of several NIH funded community-based interventions, and of a Centers for Disease Control, REACH Center grant to eliminate diabetes disparities among African Americans and Latinos. She is director of the East Harlem Diabetes Center of Excellence, Dean for Gender Equity, Director of the Institute for Health Equity Research, and the Principal Investigator of the Community Engagement and Research Core for Mount Sinai's Institutes for Clinical and Translational Sciences. She has implemented numerous community-based health improvement interventions, and mentors students, residents and faculty interested in addressing disparities and partnering with communities on research to improve local health and influence policy. Dr. Horowitz has an MD degree from Cornell University, and received an MPH from the University of Washington as a Robert Wood Johnson Clinical Scholar.

Cordelia Elaiho, MPH, is the clinical research coordinator who will assist with study participant outreach and coordination of study events. Cordelia will assist in collecting study information using electronic databases, corresponding with study participants, maintaining study files, survey administration, and consent/assent. Cordelia has completed all necessary CITI and HIPAA trainings and has filed an FCOI disclosure in Sinai Central.

Bian Liu, PhD, is an Assistant Professor in the Department of Population Health Science and Policy at Mount Sinai with many years experience working with complicated data sets. Dr. Liu will work with the research team and CAB to analyze and interpret the data and findings. She will work closely with the research team, the programmer, and the evaluation team to implement the evaluation plan. Dr. Liu will collaborate with the programmer to ensure the integrity of the

data collected. She will provide technical assistance on the analytical needs of program staff and CAB members.

Yannan Li, MD, MPH, is a Senior Data Analyst in the Department of Population Health Science and Policy at Mount Sinai with many years of experience working with complicated data sets. Dr. Li will assist Dr. Liu in analysis, data interpretation and findings. She will work closely with the research team, the programmer, and the evaluation team to implement the evaluation plan.

TBD. We will recruit potential peer leaders through our contacts at community youth organizations in East and Central Harlem. Leaders should be older than 18 years, English speaking, may be male or female and may be of any racial/ethnic background. Individuals will be interviewed and chosen based on prior leadership experience, personal interest in diabetes prevention and level of commitment. Peer leaders will attend training sessions, workshop sessions and debriefing sessions. Peer leaders will complete all necessary CITI training and a FCOI disclosure in Sinai Central prior to involvement in any study related activities.

10.1.6 SAFETY OVERSIGHT

N/A

10.1.7 CLINICAL MONITORING

N/A

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Each clinical site will perform internal quality management of study conduct, data and biological specimen collection, documentation and completion. All sites will follow a common quality management plan.

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 (see **Section 10.1.9, Data Handling and Record Keeping**) 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 in **Section 6.2.1, Interventionist Training and Tracking**.

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 clinical trial staff at the site under the supervision of the site investigator. 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) and into REDCap derived from source documents will be consistent with the data recorded on the source documents.

Clinical data (including adverse events (AEs), concomitant medications, and expected adverse reactions data) and clinical laboratory data will be entered into REDCap, a 21 CFR Part 11-compliant data capture system provided by the Icahn School of Medicine at Mount Sinai. 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 2 years after the last approval of a marketing application in an International Council on Harmonisation (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the study intervention. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor/funding agency, if applicable. It is the responsibility of the sponsor/funding agency to inform the investigator when these documents no longer need to be retained.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. 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.

These practices are consistent with ICH GCP:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1
- Section 5.20 Noncompliance, subsections 5.20.1, and 5.20.2.

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 14 working days of identification of the protocol deviation, or within 30 working days of the scheduled protocol-required activity. All deviations will be addressed in study source documents, reported to the PI. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator will be responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

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. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

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 National Institute of Diabetes and Digestive and Kidney Diseases (NIDDKD) 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

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
ANCOVA	Analysis of Covariance
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
DRE	Disease-Related Event
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
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GWAS	Genome-Wide Association Studies
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICH	International Council on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IDE	Investigational Device Exemption
IND	Investigational New Drug Application
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ITT	Intention-To-Treat
LSMEANS	Least-squares Means
MedDRA	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
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
SOC	System Organ Class
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

*The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A **Summary of Changes** table for the current amendment is located in the **Protocol Title Page**.*

Version	Date	Description of Change	Brief Rationale

11 REFERENCES

Include a list of relevant literature and citations for all publications referenced in the text of the protocol. Use a consistent, standard, modern format, which might be dependent upon the required format for the anticipated journal for publication (e.g., N Engl J Med, JAMA, etc.). The preferred format is International Committee of Medical Journal Editors (ICMJE).

Examples:

- ***Journal citation***
  Veronesi U, Maisonneuve P, Decensi A. Tamoxifen: an enduring star. J Natl Cancer Inst. 2007 Feb 21;99(4):258-60.
- ***Whole book citation***
  Belitz HD, Grosch W, Schieberle P. Food chemistry. 3rd rev. ed. Burghagen MM, translator. Berlin: Springer; 2004. 1070 p.
- ***Chapter in a book citation***
  Riffenburgh RH. Statistics in medicine. 2nd ed. Amsterdam (Netherlands): Elsevier Academic Press; c2006. Chapter 24, Regression and correlation methods; p. 447-86.
- ***Web Site citation***
  Complementary/Integrative Medicine [Internet]. Houston: University of Texas, M.D. Anderson Cancer Center; c2007 [cited 2007 Feb 21]. Available from: http://www.manderson.org/departments/CIMER/.
- ***Electronic Mail citation***
  Backus, Joyce. Physician Internet search behavior: detailed study [Internet]. Message to: Karen Patrias. 2007 Mar 27 [cited 2007 Mar 28]. [2 paragraphs]
- ***References to package insert, device labeling or investigational brochure***
  Cite date accessed, version number, and source of product information.