Study Title Power-Up: An Effectiveness Trial of the Diabetes Prevention Program
NCT Number NCT04104243
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This proposal responds to PA-16-428, "Health Promotion Among Racial and Ethnic Minority Males," with *Power-Up for Health*, an effectiveness trial of an adapted National Diabetes Prevention Program (NDPP) tailored to engage men with prediabetes and offered through primary care settings that serve disadvantaged urban communities. The rising epidemic of type 2 diabetes is a major cause of disability and death that disproportionately affects men. The burden of diabetes for men is further compounded by well-documented racial/ethnic disparities in diabetes risk, prevalence, control and health outcomes. Despite this disproportionate impact, effective diabetes prevention programs largely fail to reach and engage men. Gender disparities in NDPP participation are typically stark, with men averaging 20% of participants, although men who do participate achieve equivalent or better weight loss, compared to women. It remains mostly unknown to what extent failure to engage men in NDPP represents limited reach (i.e., proportion of the eligible population who participate) of standard recruitment efforts, typically based on physician referral, versus poor engagement (i.e., participation in and exposure to the intervention) and retention. Results from our 2-year pilot study (R18 DK102080) show that *Power-Up* can be successfully implemented and achieve similar weight loss, as compared to NDPP, but rigorous evaluation is needed.

The proposed study builds on this successful NIDDK-funded pilot work to address the clear need for a men-tailored approach to diabetes prevention. *Power-Up* is an intervention that is: a) tailored to the needs and preferences of racial/ethnic minority men; b) delivered by men coaches in men-only groups; and c) uses adapted content that highlights issues relevant to men and messaging designed to be acceptable and engaging to men. Based on the pilot results, we propose to conduct a rigorous effectiveness evaluation using a pragmatic RCT design within diverse healthcare settings already implementing standard mixed-gender NDPP. The goals of this study are to: 1) test the effect of *Power-Up* on weight loss; 2) evaluate engagement of men in *Power-Up*; and 3) examine the reach, broader effectiveness, implementation, and costs of *Power-Up* to inform future dissemination efforts and plans for sustainability.

The proposed study will leverage existing collaborations with co-investigators testing best practices for recruitment, implementation and evaluation of NDPP in a bureau of the New York City Department of Health and Mental Hygiene. Through this partnership we will recruit 300 men from across a spectrum of primary care centers - from a major urban academic medical center to small- and medium-sized primary care practices throughout New York City serving disadvantaged communities. Electronic Health Record data will facilitate outreach to the population of eligible men, based on NDPP criteria, rather than relying on physician referral, and will establish a valid denominator for the total population of eligible men, allowing for a rigorous assessment of the reach of our recruitment approach and an evaluation of the representativeness of our sample. Indicators of effectiveness, adoption, implementation and cost will be analyzed, guided by the RE-AIM framework.

Aim 1. Assess the effect of *Power-Up* vs. NDPP on weight loss among racial/ethnic minority men at risk for diabetes.
Hypothesis 1 (Primary Outcome): Men randomized to *Power-Up* will achieve significantly greater weight loss at 16-weeks and 1-year than men in the standard care group referred to mixed-gender NDPP classes.

Aim 2. Compare engagement of racial/ethnic minority men at risk for diabetes in *Power-Up* vs. NDPP.
Hypothesis 2 (Secondary Outcome): Men randomized to *Power-Up* will have significantly greater engagement rates (i.e., attend at least 4 sessions) and retention rates (i.e., attend 9 or more sessions) than men randomized to standard care and referred to mixed-gender NDPP classes.

Aim 3. Evaluate the Reach, Effectiveness, Adoption, Implementation, and Costs of *Power-Up*.
(Exploratory outcomes) Use the RE-AIM framework to evaluate: 1) the reach of our recruitment methods and the representativeness of men who enroll in the study, are successfully engaged, and who are successfully retained in *Power-Up* vs. standard NDDP, relative to the eligible population; 2) the broader effectiveness of *Power-Up* based on patient-reported outcomes [e.g., self-reported health, health behaviors, psychosocial factors] and routinely measured clinical data [e.g., change in blood pressure, change in HbA1c]; 3) adoption of *Power-Up* at the practice level; and 4) the fidelity and consistency of implementation and total program costs of *Power-Up*.

Recruitment and Retention Plan

RECRUITMENT STRATEGY. We will select sites based on availability of virtual NDPP classes. As the sessions are taking place virtually the site does not need to be near the participant. Having the Prevention Outreach Specialist at PCIP/DOH trained as a Master Trainer will ensure we are able to support NDPP efforts at PCIP/DOH small and medium sized practices over time, by training additional NDPP coaches if necessary. We expect a high rate of participation among approached practices, based on our experience in *NYC Care Calls* where 11 out of 12 approached practices agreed to participate. To offset some of the burden of participating in a study such as this for small and medium sized practices that may not have the resources and larger institutional support for research, we have budgeted $1000 stipends for each participating practice in the PCIP/DOH network. We expect to engage approximately 20-30 practices across the two partnering healthcare systems to meet our recruitment goals. We will also contact eligible participants within Montefiore Medical Group.

After securing an agreement from a given practice, we will use EHR search capabilities to generate lists of men who: 1) meet all of the following NDPP criteria based on EHR values– at least 18 years old, most recent BMI ≥ 25 (within last 6mos), most recent HbA1c: 5.7%-6.4% (within last 12 months); and 2) received care at a NYC-based PCIP health care clinic in the past 12 months. A physician from the practice will have the opportunity to review these lists and exclude any patient they deem inappropriate for participation based on serious mental illness, dementia or other cognitive problems, or physical disability that would prevent attendance and participation in the intervention sessions or telephone surveys. Reasons for exclusion will be recorded and coded systematically. Participants will be contacted via phone without sending an opt-out letter. PCIP/DOH and Montefiore Medical Group (MMG) participant outreach does not mail letters to participants in standard care therefore they will be contacted as they are contacted normally.

To be fully eligible, men must: 1) have no plans to change their primary care provider or move from their current address in the next year; 2) must agree that they are able and willing to attend virtual, group-based diabetes prevention classes; 3) must complete the baseline survey assessment and be willing to complete follow-up study surveys and procedures for collecting study weights; and 4) must provide informed consent by telephone, including consent for study participation, data collection, and random assignment to *Power-Up* or standard care NDPP. These methods for recruitment, eligibility screening, and oral consent have been previously approved by the NYC DOHMH and the Albert Einstein College of Medicine IRBs and are based on our successful recruitment for the NYC Care Calls Study (R18 DK 09742), conducted in partnership with PCIP.

Since there are likely to be 30,000-40,000 men patients across all of the PCIP/DOH and MMG practices who meet the eligibility criteria, we will be unable to call and screen all at once. Instead, we will target a small number of particular practices at a time, closing recruitment at these sites and moving on to other practices as we exhaust the full population of potentially eligible men at each site. We will also limit contact to those men who have had their weight measured within the last 6 months to limit the possibility that men will no longer be eligible for the programs based on weight and to increase the precision of our estimates for missing study-weights in the case of missing data or loss to follow-up. Our recruitment procedures represent a departure from current NDDP recruitment practices at PCIP/DOH and MMG practices, which rely on physicians to identify eligible patients and refer them to the NDPP. We expect that this active outreach approach will allow us to reach our recruitment goal of 300 enrolled participants given the large population of potentially eligible patients available through our health system partner. Given that we will not reach all practices in these networks, we will also be able to compare the reach and representativeness of our male sample across both arms of the trial, using EHR-based outreach, to that achieved by non-participating practices within our healthcare system partners' networks that continue to rely on physician referral for recruitment into NDPP.

RETENTION STRATEGIES. Our retention strategies are informed by our experience with the pilot and prior health behavior change and lifestyle intervention studies conducted by our team involving longitudinal follow-up of participants over 12 months or more. Based on this experience, we will provide monetary incentives for completion of telephone-administered surveys and for presenting for the collection of weights at the designated intervention session (e.g., 16 weeks and 12 months), which will be mailed to participants via the use of Clincards. We will also send reminders via text message, email, and/or mail for all first session, 16-week and 12 month weigh-ins, across both arms of the study. In addition, we will send cards in the mail to keep rapport by acknowledging birthdays and holidays and updating participants of the study. Participants will be supplied with scales to track their weight remotely.

Development of study branding with a graphic designer to be used in all study communications and materials and sending periodic mailings to participants to remind them of upcoming appointments for surveys or weight-collection will also be helpful in fostering a sense of ongoing participation and helping participants keep their appointments. Bonding of participants within groups is one of the most important retention strategies promoted by the coaches. For example, buddy activities and raffle ticket giveaways during the class sessions have improved group cohesion and class retention in prior DPP efforts. Well-trained coaches who are cognizant of retention issues are likely the most effective strategy to reduce attrition. Coaches use texts and email in addition to phone calls to remind participants of upcoming sessions, address missed sessions and troubleshoot issues that come up regarding attendance. For example, when a participant misses a session, the coach will typically text and call the participant to make up the session via telephone and identify barriers to getting to session. Session scheduled times conflicting with work schedules and family commitments are the most common barriers identified. Thus, we have planned to hold sessions mostly in the evenings, with weekend sessions also available. Information from our baseline survey can also be used to help inform common reasons why a participant may miss sessions (e.g., childcare or complex work schedule). Participants will be contacted via text (with their permission) reminding them to complete study questionnaires, weigh-in prior to sessions, fill out their physical activity logs, and the link for joining the sessions.

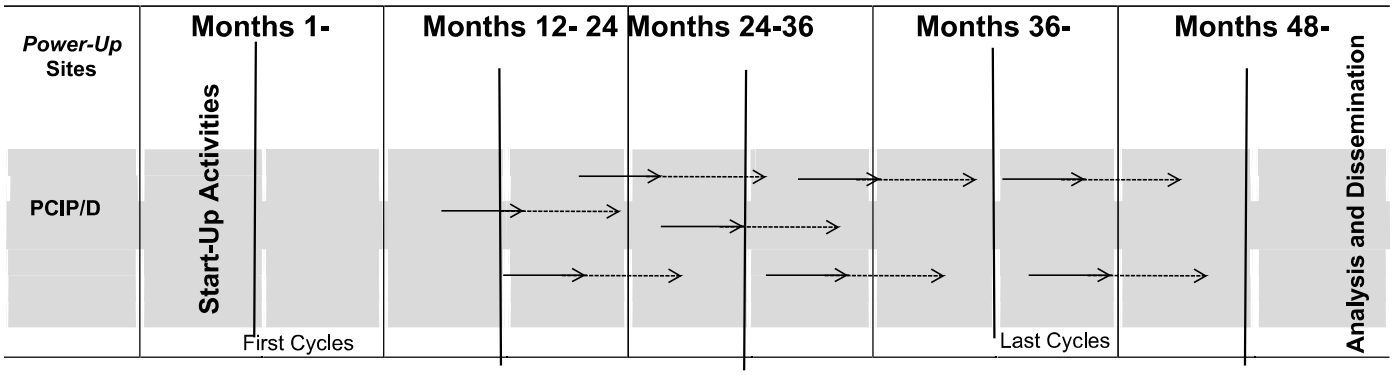
PHS HUMAN SUBJECTS AND CLINICAL TRIALS **STUDY TIMELINE**

We have planned our study to ensure sufficient time to recruit and follow-up our 300 participants before a 6-month period at the end of the study that will be concentrated on data analysis, writing-up of results, and dissemination. To achieve this goal, we will begin recruitment and implementation of the assessment and intervention procedures of the study at month 6 of the first year of funding. The first 6 months of the first year will be focused on hiring of staff, study-start-up, ordering of materials, setting-up databases for study variables, finalizing data extraction protocols, finalizing qualitative interviewing questions and procedures, and, finalizing procedures and intervention content in consultation with our expert Advisory Board. We have sufficient time to meet our study milestones and recruitment goals and plan time the cycles of intervention to ensure successful progress. The study will last 60 months, with start-up activities taking place in months 1-6. Intervention Cycles will run simultaneously between the 2 intervention settings over a 3-year period of the award. We will recruit 300, run 8 intervention cycles of approximately 40 men randomized 1:1 to each arm in months 13-54. Follow-up 16-week and 12-month assessments will be completed in months 24-54. Data analysis and dissemination activities will take place in months 55-60. Our budget allows us to hire 8 coaches in year 1 and up to another 8 coaches in year 3, ensuring our ability to run a sufficient number of groups.

Study Activity Timeline

Study Activity	Year 1		Year 2		Year 3		Year 4		Year 5	
Meetings with Advisory Board										x
Train coaches in implementation and data collection			x		x					
Recruitment data abstraction, mailings & outreach			x	x	x	x	x			
Baseline weight assessment and surveys			x	x	x	x	x			
Implement *Power-Up* sessions			x	x	x	x	x	x	x	
Observe *Power-Up* and DPP sessions for fidelity				x	x	x	x	x	x	
Practice Exit Interviews				x	x	x	x	x	x	
Follow-up weights and surveys (16 wks and 12 mos)				x	x	x	x	x	x	
Participant focus groups and individual interviews				x	x	x	x	x	x	
Lifestyle coach surveys				x	x	x	x	x	x	
Lifestyle coach interviews				x	x	x	x	x	x	
Analyses, publications, and reports for dissemination										x

Intervention Cycles Timeline



Each cycle consists of a 16-week core phase to be completed within 6-months ( ) and six-month post-core maintenance phase of 6 sessions ( ). The duration of each cycle is 10-12 months.
Concurrent with each Power-Up Cycle, a similar number of NDPP sessions will be available for men assigned to the standard care, mixed-gender NDPP condition.

Inclusion Enrollment Report 1

Using an Existing Dataset or Resource* : ○ Yes ● No

Enrollment Location Type* : ● Domestic ○ Foreign

Enrollment Country(ies): USA: UNITED STATES

Enrollment Location(s): Domestic; primary care clinics in NYC

Comments: Entries reflect totals recruited across Montefiore and PCIP/ NYC-DOHMH sites

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	3	0	3	6
Asian	0	6	0	5	11
Native Hawaiian or Other Pacific Islander	0	1	0	0	1
Black or African American	0	71	0	62	133
White	0	70	0	63	133
More than One Race	0	5	0	11	16
Total	0	156	0	144	300

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0

PROTECTION OF HUMAN SUBJECTS

1. Risks to Human Subjects

1a. Human Subjects Involvement, Characteristics, and Design. We will evaluate our Aims within a healthcare system that is implementing the NDPP as a standard of care via a practical two-arm randomized controlled trial (RCT), where eligible men are randomly assigned to receive either *Power-Up* or standard, mixed-gender NDPP.

The study will be carried out by Albert Einstein College of Medicine (AECOM) and PCIP/NYC-DOHMH-based study staff. A co-investigator from PCIP/DOHMH, Ms. Jill Linnell is participating in this proposal and will have responsibility for engaging primary care practices based on their knowledge of the practice population and preliminary searches of electronic databases. Practices that have well established procedures for referring to the NDPP and that have access to robust NDPP programming in English and Spanish will be prioritized to ensure equipoise of the RCT arms with respect to exposure to intervention. Practices serving large numbers of Black, Hispanic, and/or Spanish speaking patients will also be prioritized.

Study Sites	Site Investigators
Albert Einstein College of Medicine	Earle Chambers, PhD, MPH (PI) Jeffrey Gonzalez, PhD (PI) Elizabeth Walker, PhD, RN, CDE (Co-I) Clyde Schechter, MD (Co-I)
Primary Care Information Project/New York City Department of Health and Mental Hygiene	Jill Linnell, MPH (Co-I)

Participant eligibility will be ascertained by PCIP and AECOM staff. Based on electronic health record (EHR) searches, we will generate lists of men who: 1) meet all of the NDPP criteria – at least 18 years old, most recent BMI ≥ 25 (within last 6mos), most recent HbA1c: 5.7%-6.4% (within last year); and 2) have valid address and telephone contact information. Participants will be contacted via telephone without receiving an opt-out letter. To be fully eligible, men must: 1) have no plans to change their health system or move from the NYC area in the next year; 2) be physically able and willing to attend virtual, group-based sessions; 3) complete baseline phone surveys and be willing to complete follow-up surveys and procedures for collecting study weights (See C.8.a of Research Strategy); and 4) provide informed consent by telephone. These methods for recruitment, eligibility screening, and oral consent have been previously approved by the AECOM IRB and are based on our successful recruitment for *NYC Care Calls* (See C.2.e of Research Strategy).

1b. Study Procedures, Materials and Potential Risks.

Study procedures will primarily take place in our study offices at AECOM and PCIP/NYC-DOHMH and at local sites of participating practices from the PCIP and MMG networks. Additional procedures for weight collection, when participants do not attend intervention sessions where weights are primarily measured, may take place at additional sites. Recruitment, eligibility screening, and enrollment procedures will be conducted by research assistants/prevention outreach specialists located at our AECOM and PCIP/NYC-DOH offices. Potentially eligible men will be: via telephone follow-up; informed of their risk for diabetes and the availability and efficacy of the DPP; evaluated for eligibility; asked to provide oral informed consent by phone; and then randomized to one of the two conditions. Random assignment will be conducted using envelopes with the randomization condition inside. The research coordinator will have access to the envelopes. Study coordinators will contact the research coordinator who will tell the SC which condition the participant will be receiving. Randomization will occur at AECOM for all participants. Random assignment, and final enrollment into the study will occur after telephone screening, and completion of baseline surveys. With leadership from Dr. Elizabeth Walker (Co-I), all

coach training for *Power-Up* intervention delivery will occur in AECOM or PCIP/NYC-DOHMH meeting space. NDPP training for coaches will occur through established programs.

Materials for the study include digitally measured weight (via GSM connected BodyTrace scales), intervention session attendance records, EHR-16
clinical data, survey responses, digital recordings of individual interviews, and focus groups, and fidelity ratings from coaches, as well by the PIs, based on observation of sessions.
These materials will be collected using internet connected scales, by telephone or by remote search of EHR systems by staff based at our study offices. *Power-Up* sessions (16 core sessions delivered over 6 months and 8-10 additional maintenance sessions delivered over the subsequent 6 months for a total of 24 sessions over one year) will also be conducted virtually. Participants will be given the sessions digitally or a paper copy will be mailed out to them upon request. All participants will receive activity, food and weight logs by mail. Participants will also receive a handout on applications and action plans. Surveys of validated self-report questionnaires for psychosocial and behavioral variables will be conducted by telephone by study staff at our AECOM and study offices. These surveys will occur at baseline/enrollment (immediately prior to randomization), at approximately 16-weeks (goal to conduct this survey within a window of +/- 1 month of the 16-week intervention session), and 12-months (goal of +/- 1 month of the 12-month final maintenance session). Surveys may also be conducted by phone, where necessary (e.g., meeting a participant who missed a session to collect weight and administering the survey of self-reports in person, via the same procedure of reading the questions and response scales to the participant, as implemented during telephone administration). Study staff and trained coaches will collect and manage all primary data. Study staff will review coach-collected data on weights, heights, and attendance, as well as coach-completed fidelity checklists, for quality assurance, providing immediate feedback through prompt communication with coaches, by phone, text or in-person to address any quality issues. Protocols for qualitative data collection will be finalized with guidance from Dr. Linda Weiss (Consultant) and recordings and transcripts will be securely stored at our study offices. Daily activities of staff will be managed by an onsite project manager at each study office site. All staff will be trained, overseen and advised by Drs. Chambers and Gonzalez (PIs). The control arm weight and attendance data collection of men assigned to standard care NDPP will be supervised by Dr. Chambers and for PCIP by Dr. Gonzalez in collaboration with Ms. Linnell (PCIP, co-I).

The primary outcome measure will be percent change in weight at the end of the Core (16 weekly) sessions and at the end of 12 months. We will examine several process and moderating variables, based on a telephone survey of self-report measures validated for English and Spanish language and in-person and telephonic administration, as well as EHR-extracted clinical variables, such as A1c, blood pressure, lipids, etc. 6 months after the delivery of the final session weights will also be EHR-extracted from clinical visits during the 1-year trial period, the 6 month wait is to allow for the updating of EHR data. Extracting these weights will help us capture weights for those who never attended sessions. Coaches will record , weight (using wireless internet connected scales), session attendance logs via study- ID coded and de-identified data entry. They will also complete fidelity checklists. Both of these data entry protocols will be supervised for quality control by study staff. Staff will also track and keep records of all study- related costs. These records will be reviewed periodically by the project managers of each site and by Dr. Schechter (Co-I). Through coach surveys, coach interviews and participant individual interviews and focus groups, we will examine perceptions of *Power-Up*, fidelity to the model, barriers and facilitators to implementation and engagement, and recommendations for improvement. Participant identifying information will only be known to the primary study staff. Identifying information will be stored separately from study data in locked file cabinets in our study offices. Data will not be shared between study staff of participating health care systems and de-identified data for *Power-Up* participants will be shared with the *Power-Up* data analyst (Dr.
Schechter, Co-I) for analysis.

Potential risks of participation are minimal and include the possibility that some participants may feel uncomfortable answering questions, or talking about their weight, food habits, physical activity, and factors that affect behavior. The intervention does not convey more than minimal risk and there is no reason to suspect that any serious adverse events will be attributable to it. All participants will be strongly encouraged to speak to their health care provider about safe and appropriate levels of exercise, as they would for any change in

physical activity. The NDPP guidelines recommend increasing physical activity at a moderate level, such as brisk walking, but participants will choose their own activity outside of the Core and post-Core learning sessions.

Expression of intent to harm self and/or others. The study will not assess intent to harm self or others, however, though this is a low risk, subjects may express thoughts of harm to self and/or others while completing study questionnaires, especially as it relates to managing their pre-diabetes. Staff and coaches will be trained on how to appropriately respond to expression of intent to harm self or others, and will maintain a Manual of Procedures (MOP), which includes state law requirements and local emergency phone numbers. Healthcare providers can also be alerted about concerns regarding risk, with the participant's consent.

Other Risks. Taking part in this research study may involve providing information that participants consider confidential or private, including thoughts of harm to self and/or others. Coaches and study staff will be trained in emergency procedures for adverse health events that may occur by chance when they are interacting with participants. They will not provide any intervention themselves but will be trained to identify emergency situations (e.g., cardiac arrest) and in procedures to access emergency care (e.g., calling 911). In addition, there is a slight risk of a breach of confidentiality. Subject will be informed of confidentiality limitations in the informed consent. As described in detail below, every effort will be made to keep participant names and contact information secure; only research staff will have access to linked contact information and study data. Identifiers will be excluded from any participant data analyzed by the AECOM-based data analysts.

Alternative Treatments and Procedures. The alternative is for potential subject to not participate in the study. If potential participants decline to enroll in the study but express interest in accessing NDPP, we will inform them of the procedures to do so. All potential participants will be receiving care from sites that provide access to the NDPP.

2. ADEQUACY OF PROTECTION AGAINST RISKS

2a. Informed Consent. Study staff who have undergone human subjects training and who are approved by our IRB will obtain oral informed consent from participants by phone, after completing eligibility screening. Because of the nature of the study design, it is not feasible to consent participants in person. Creating a need to attend a study visit outside of attendance of *Power-Up* or NDPP sessions would create a barrier to participation that detracts from our efforts to ensure a generalizable sample that is representative of men who participate in Diabetes Prevention Programs. Obtaining consent at the first intervention session is not practical because it would further distort the sample's representativeness of the population of interest by limiting the sample to those who successfully attend the first session of these interventions. This would also be a threat to internal validity, as it would artificially equate the two interventions on attendance of the first session. Based on our IRB's prior approval of the oral consent procedures for other studies, including the soon to be complete *NYC Care Calls*, conducted in partnership with PCIP/NYC-DOHMH, we are confident that oral consent procedures will be approved for the current study. Our study also meets all of the Federal requirements (45 CFR 46) for waiver of written consent: (i) the research involves no more than minimal risk to the subjects; (ii) the research could not practicably be carried out without the requested waiver or alteration; (iii) the waiver or alteration will not adversely affect the rights and welfare of the subjects; and (iv) whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

Oral consent by telephone will include all of the following steps:

- All aspects of the study, as described in the consent form, are first discussed with the potential participant. The consent form is thoroughly reviewed and answers to the potential participant's questions are provided.
- After reviewing the consent form by phone, the staff person obtaining consent will verbally assess the individual's comprehension of the research and what it means to participate, including understanding of the voluntary nature of participating. Individuals will be asked to answer the following questions: (1) What are you being asked to do? (2) What question is this study trying to answer? (3) What are the potential risks of participating in this study? (4) How often will you need to come in for study visits? (5) What is the difference between participating in this study and your standard medical care? (6) What should you do if you decide to withdraw from the study?
- If the participant does not demonstrate sufficient capacity to answer the questions about the study and thus may not be able to provide informed consent, this will be documented and the participant will be excluded from study participation.
- Upon request a copy of the consent information sheet will be mailed or emailed to the participant once enrolled by the study staff. A record of completed oral consent and mailing of the printed consent document, which will include an instruction to call the study offices if the participant has any questions after reading, will be recorded in each individual's study files, which will be stored in a secure location.

Potential participants who do not have capacity to provide consent will be provided with information about how to access the NDPP through talking with their provider who would discuss whether the program may or may not be appropriate for them. Potentially eligible subjects will be invited to participate, consented, randomized to a study arm and either directed to the *Power-Up* intervention coordinator or to the NDPP coordinator at PCIP depending on the patient's health care home. The consent document will include information about study procedures, including that participants will be randomized to either standard NDPP or *Power-Up*, that they will be contacted by telephone, email (if applicable) and mail for follow-up surveys, and the risks and benefits of the intervention. We will ask for permission to leave telephone messages, without identifying the exact purpose of the call, when we are making study-related calls. We will also ask for permission to send text messages via the coaches as reminders for sessions and questionnaires. Participation in the proposed study will be completely voluntary. Prospective subjects will be told that a decision to decline participation will not affect their health care.

The proposed research will follow the Health Insurance Portability and Accountability Act of 1996 (HIPAA) guidelines for protecting the privacy and documenting informed consent of participants. Intervention recruitment, consent, and enrollment will not begin until the study receives approval from the AECOM IRB, as outlined in the Consortium of Informed Consent Section.

Databases will be secured with encryption and use of secure serves. The REDCap data management system is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. The REDCap website is password-protected and restricted to users who have been authorized to gain access. The site employs a multi-level authorization structure where certain areas are available to all authorized users and other areas available only to specified users. Within each area there are different levels of authorization related to whether an individual has 'view only' privileges or has 'data entry' privileges. We have access to REDCap without a need to charge the current study's budget through AECOM.

2b. Protection Against Risk. Every effort will be made to prevent a breach of confidentiality. Individuals who enroll in the study will be assigned a unique ID number. All study data will be maintained with the IDs rather than names or identifiable information. *Power-Up* study director will keep a log linking the ID number to identifiable contact information for follow-up purposes. The log will be maintained on a password-protected

directory accessible to the *Power-Up* research staff only.

Data will be collected using 1) hard copy surveys until we finalize the online database (REDCap); and 2) digitally recorded in-person and telephone interviews and focus groups.

- Surveys will be administered primarily over the phone and occasionally in person (when pursuing missing data) by the study staff. Data will be entered from hard copies into the confidential study database by the study staff.
- Interviews and focus groups will be facilitated by the study staff and/or graduate students and post-doctoral fellows in Clinical Health Psychology, working in Dr. Gonzalez' research lab; they will be audio recorded using a digital recorder. Interview recordings will serve as backup to notes. Focus group recordings will be professionally transcribed. Recordings and typed transcripts will be transmitted via the secure FTP server. The transcriber will sign a confidentiality agreement, attesting to the fact that data in the recordings will remain private. These qualitative interviews and focus groups, administered after participation in the main study activities, will utilize a consenting process that is separate from and supplementary to the process for the main study, and will be completely voluntary.

- The study staff will ask the study participants to only use their first name when they joining a virtual sessions, suggest to turn off their camera, and ensure that the virtual sessions are not recorded. If the participant is joining via phone, the staff will ask them to join privately. If the participant chooses not to follow these instructions, they will be expose to potential security risks.

Hard copy documents, including locator forms and surveys, will be stored in locked file cabinets at AECOM, accessible only to the *Power-Up* research team. Forms with identifying information (e.g. consents) will be stored in a different cabinet from the completed surveys and any other study data. All electronic data will be stored at AECOM on password-protected drives that are backed up daily. Hard copy and electronic data will be accessible to study staff only.

After data collection is complete, the research team will agree on the parameters for de-identifying this data (e.g. choosing among top or bottom coding, adding random noise, stochastic data interchanges, or other methods) to adequately protect participants' confidentiality. The de-identified demographics file, linked to the survey results and weight and activity tracker will be used by the *Power-Up* data analyst for specific preliminary and final analyses.

Provisions for ensuring necessary medical or professional intervention in the event of adverse effects will be coordinated through Dr. Walker, but will follow usual PCIP procedures. Adverse events reported directly by lifestyle coaches will be referred directly to Dr. Chambers. He will also monitor the de-identified data collected on an ongoing basis to ensure the safety of subjects enrolled in our study. We feel that these measures are adequate to protect against risk.

Expression of intent to harm self and/or others. Subject will be informed during consenting about the limits to confidentiality if intent to harm self and/or others is expressed. Study staff shall assess a subject's expression of harming self and/or others. Harm deemed imminent shall be immediately reported to the local authorities as required by state law. Staff will note alert in chart and notify the subject's primary care provider. Intent to harm self and/or others shall be recorded as a Serious Adverse Event at the local and coordinating center IRB. Because surveys will primarily be conducted by phone, we will use the PHQ-8 scale to assess depressive symptoms (See Table 1, Research Strategy), rather than the PHQ-9, to avoid directly inquiring about suicidal risk. Given the target population, true imminent suicidal risk is expected to be exceedingly rare and asking questions about suicidal ideation would mostly yield false positives. However, all staff will be trained in suicidal risk assessment by Dr. Gonzalez, a licensed clinical psychologist in NY State, and will be trained in a protocol of how to respond to risk with referrals for mental health care at one end of the spectrum of risk and calling 911 and/or crisis response teams at the other.

Breach of confidentiality. Study participants face risks related to inadvertent release of confidential information.

This will be minimized through careful adherence to best practices for data collection and management. All research staff will be trained in principles and methods for assuring participant confidentiality and safety. Efforts, such as keeping research records secure and allowing only authorized people to have access to research records, will be made to keep the information safe. Participants will be given any new information we become aware of that would affect their willingness to continue to participate in the study.

Data will be used only in aggregate and no identifying characteristics of individuals will be published or presented. Results of assessments will be sent to participants' care providers only if participants agree to this. Confidentiality of data will be maintained by using research identification numbers that uniquely identify each individual. Safeguards will be established to ensure the security and privacy of participants' study records. Databases will not use participants' names as identifiers: a research ID number will be used. The research records will be kept in a locked room in the study offices. The files matching participants' names and demographic information with research ID numbers will be kept in REDCap with restricted access. Only study personnel will have access to these files, and they will be asked to sign a document that they agree to maintain the confidentiality of the information. After the study is completed, data will be stored with other completed research studies in a secured storage vault.

Consent will cover the use of confidential data collected by the study and will permit sharing these data among, incorporation in the study databases, and the distribution of de-identified data for public use databases. If required, an NIH Certificate of Confidentiality will be sought prior to be beginning of recruitment to offer further protection of privacy. Limits to confidentiality as it relates to expression of intent to harm self and/or others shall be included in the informed consent.

3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

The potential benefits of the proposed research involve learning about ways to effectively engage men in diabetes prevention programs. The NDPP has been shown to promote weight loss and reduce risk of diabetes. As all participants will have access to the core content of the NDPP, across both arms of the trial, all participants may benefit from accessing it. However, it is possible that participants will not experience weight-loss through participation and may not derive direct benefit for themselves. Nevertheless, accomplishing our Aims, as outlined below will generate knowledge that may promote the wide dissemination of our approach, if effective, potentially benefiting healthcare systems, the population of racial and ethnic minority men at risk for diabetes, and contributing to a reduction in gender and racial/ethnic health disparities.

Aim 1. Assess the effect of Power-Up vs. NDPP on weight loss among racial/ethnic minority men at risk for diabetes. Hypothesis 1 (Primary Outcome): Men randomized to *Power-Up* will achieve significantly greater weight loss at 16-weeks and 1-year than men in the standard care group referred to mixed-gender NDPP classes.

Aim 2. Compare engagement of racial/ethnic minority men at risk for diabetes in Power-Up vs. NDPP.

*Hypothesis 2 (Secondary Outcome): Men randomized to Power-Up will have significantly greater eng*agement rates (i.e., attend at least 4 sessions) and retention rates (i.e., attend 9 or more sessions) than men randomized to standard care and referred to mixed-gender NDPP classes.

Aim 3. Evaluate the Reach, Effectiveness, Adoption, Implementation, and Costs of Power-Up. (Exploratory Outcomes) Use the RE-AIM framework to evaluate: 1) the reach of our recruitment methods and the representativeness of men who enroll in the study, are successfully engaged, and who are successfully retained in *Power-Up* vs. standard NDDP, relative to the eligible population; 2) the broader effectiveness of *Power-Up* based on patient-reported outcomes [e.g., self-reported health, health behaviors, psychosocial

factors] and routinely measured clinical data [e.g., change in blood pressure, change in HbA1c]; 3) adoption of *Power-Up* at the practice level; and 4) the fidelity and consistency of implementation and total program costs of *Power-Up*.

4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

Results from this study will 1) increase knowledge about how to engage and retain men in health promotion programming, 2) inform the development of future interventions to prevent diabetes among men, 3) provide much-needed data regarding the incremental effect of a targeted prevention program for men, 4) help inform public health policy regarding the costs and benefits of alternative interventions to reduce the incidence of diabetes. The risk-benefit ratio in the proposed study is acceptable for the following reasons. First, all enrolled individuals will be at high risk for diabetes and will participate in an evidence-based intervention, with proven effectiveness. Second, all participants in the *Power-Up* model will receive a tailored program that has shown to be acceptable to men and may improve engagement and weight loss outcomes.

Contact PD/PI: Chambers, Earle

Data and Safety Monitoring Plan

This study is a Phase III Clinical Trial of a behavioral intervention being tested in a translational, randomized controlled trial for with prediabetes. Information on the study will be provided to participants by telephone, in writing via mail, and in person. The intervention does not convey more than minimal risk, and there is no reason to suspect that any serious adverse events will be attributable to it. The most serious risk connected with the study is a potential breach of confidentiality. The Data and Safety Monitoring Plan will address risk and will outline procedures for reporting adverse events that may be expected from participants ≥ 18 years old with prediabetes, even though no such events are expected to be attributable to the intervention. Dr. Chambers will assume the responsibilities for data and safety monitoring for this study. All co-investigators and staff will cooperate with Dr. Chambers to provide all necessary data for this task in the event of any adverse events. Drs. Chambers and Gonzalez, as co-PIs, are fully responsible for the system remaining intact. Dr. Chambers will periodically (at least bi-annually) assess and review data collection and storage procedures at both sites to ensure that confidentiality is being maintained.

Adverse Event Monitoring. Participants who miss sessions will be contacted by their coach. If the coach is informed that the participant is hospitalized or deceased, the coach will report that information to AECOM or PCIP/NYC-DOHMH project manager immediately, who will in-turn report it to Dr. Chambers. The two follow-up surveys (after completion of 16 Core sessions, and after completion of 6 maintenance sessions) also include questions about hospitalizations and other serious adverse events. These surveys will be administered primarily by telephone by our research staff based at our two sites and occasionally in person, when meeting participants to collect missing weights who have also been non- responsive to attempts to schedule a telephone survey, using equivalent procedures to those used for telephone administration. If, 1) the interviewer is informed of an adverse event in the course of the survey, or 2) while trying to reach the participant, the interviewer is informed by someone in the household of a subject's hospitalization or death, that event will be noted. Any hospital admission for a related condition or death from any cause will be immediately reported to Dr. Chambers who will record them. The Einstein IRB will maintain reports of adverse events.

Information about adverse events will be sought as described above. Unanticipated (non-serious) adverse events will be reported to the IRB within 30 days of such an event using the AECOM IRB Adverse Event Report. Serious adverse events will be reported to the IRB within 48 hours by phone and email. A completed AECOM IRB Adverse Event Report will be submitted within 10 days of initial IRB notification. All deaths will be reported to the IRB within 48 hours of ascertainment. The monitor will maintain a file of all ascertained adverse events that can be used to submit summary reports.

Recruitment Monitoring. Once initial recruitment begins, the study director will compile a weekly and cumulative tally using study identification numbers of recruited and randomized subjects. Drs. Chambers and Gonzalez and co-Is will assess on a bi-yearly basis the feasibility of reaching projected recruitment targets based on interim recruitment and retention reports. Regarding retention, all recruited participants will be included in the analyses on an intention-to-treat basis unless they request to be dropped from the study specifically. Participants 1) requesting only an end to the intervention, 2) who cannot be contacted or 3) for whom outcome measures are not available, will be included in the analysis for outcome measures that are available. These latter subjects will not be considered drop-outs for purposes of retention statistics.

Data Safety and Monitoring Board. Dr. Chambers will have primary responsibility for ongoing monitoring of data related to safety for this study on an on-site, day-to-day basis. He will consult regularly with Dr. Gonzalez on the results of his monitoring to discuss any concerns related to safety or the integrity of the study.
However, because this is a Phase III Clinical Trial, we will also establish an independent Data Safety and Monitoring Board (DSMB) to oversee the activities of our research trial in order to ensure the safety of participants, the validity of our findings, and the need for further data collection. We propose a DSMB membership that may include a statistician, an expert in diabetes prevention program research, and a

healthcare provider with experience and expertise in the care of prediabetes and diabetes. All of these individuals will also have experience and expertise in the conduct of Phase III Clinical Trials Human Subjects Research. The PIs and investigators will interact with the DSMB at the DSMB's discretion, providing them with material to facilitate fulfillment of the functions detailed below. These include:

1. Review of protocols, informed consent procedures, and safety plans.
2. Monitor the progress of the intervention, i.e. participant recruitment and retention, risk/benefit ratio for participants, adherence to timetable, and quality of data.
3. Evaluation of the impact of new treatment developments on the risk/benefit ratio of our study.
4. Make recommendations to the PIs about continuation, modification, or termination of the intervention based on adverse events or beneficial outcomes.
5. Request interim analyses.
6. Monitor the confidentiality of the intervention data and the results of monitoring.
7. Offer consultation to the investigators on procedures likely to increase participants' burden, to raise ethical concerns, or to give the appearance of conflict of interest.

<u>The following data will be available to the DSMB Board:</u>

1. All adverse events: We are required to report in writing adverse events to our IRB within 48 days from the time that we become aware of an adverse event. The adverse event forms will be made available to the DSMB as well as tables summarizing the occurrence of specific events; such tables can help identify the systematic occurrence of an adverse event and lead to protective measures. As we are already required to report each event to our IRB, we plan to report to DSMB these adverse events and updated summary tables within 48 hours from each adverse event.

2. Any analyses requested by the DSMB Board.

3. Manuscripts and publications.

The DSMB will convene at least once annually, and more often as needed, either in person if logistically feasible, or by phone/Zoom video conference. The meeting will begin with a progress report by the PIs, followed by a report on any adverse events from Dr. Chambers. We will then discuss interim results on Reach (characteristics of those who participate vs. refuse), Representativeness; Adoption (percent of practices approached who agree to participate), and Implementation (consistency of study recruitment and assessment procedures, fidelity checklist ratings from coaches and fidelity ratings based on observation by Drs.
Chambers and Gonzalez, any modifications to the protocol for implementation, etc). To preserve investigator blinding of outcomes that may bias their interpretation of data or approach to the protocol, interim data on Effectiveness will not be reviewed by the investigators or the DSMB, unless specifically requested by the DSMB due to safety concerns. The DSMB will conclude the meeting without the investigators present and will make a recommendation about continuation of the study.

Early Termination. Dr. Chambers and Dr. Gonzalez will determine if the study is to be terminated prior to the scheduled study conclusion, in consultation with our DSMB. Early study termination will be considered in the event of a pattern of unanticipated serious adverse events determined to be possibly, probably or definitely related to the intervention or the data collection. In such a case, interim assessment would also be considered to ascertain if the events were associated with the intervention. In the absence of a pattern of unanticipated serious adverse events, given the minimal risk character of the intervention of this study, traditional statistical stopping rules for efficacy or safety of the intervention would not be applicable. However, early study termination will be considered if:

- subject recruitment falls below 20% of the projected number of subjects 6 months after the initiation of all stepped and potential recruitment strategies have been utilized, or
- if we fail to retain (as defined above) at least 70% of enrolled study subjects at any annual review.

Dr. Chambers will consult with Dr. Gonzalez, come to agreement, seek consultation from the DSMB, and report a decision to terminate the study early to the IRBs within 48 hours of the determination and a narrative description of the reasons for early termination within 10 days.

Overall Structure of the Study Team

The study team will be led by Drs. Gonzalez and Chambers (PIs), who are both based at Albert Einstein College of Medicine. Our AECOM study offices will house a project manager and two study coordinators who will have primary responsibility for conducting and overseeing all research activities related to participants recruitment and workshop. Drs. Elizabeth Walker and Clyde Schechter (Co-Is) are also based at AECOM.

At PCIP/DOHMH Ms. Jill Linnell will oversee activities related to practice engagement, participant recruitment, assessment, and intervention delivery to participants recruited from PCIP-affiliated primary care practices. She will be supported by a full time onsite research assistant in our PCIP-based study office. She will coordinate regularly with the Einstein-based project manager and receive regular supervision from Dr. Gonzalez to ensure consistency of procedures. Together, this team will provide input to the study plans and procedures from both Einstein and PCIP/DOHMH.

All *Power-Up* coaches will be hired by the Einstein site. These coaches will be dedicated to deliver *Power-Up* PCIP-affiliated practices throughout New York City. The Einstein-based research staff will also coordinate their efforts with the research staff based at PCIP and provide support as needed.

All supplies and materials will be purchased by the Einstein site and delivered as needed to PCIP. All administration of PCIP-related expenses, outside of personnel costs for study staff, will also be carried out by our Einstein staff to maximize efficiency.

Dr. Schechter will develop procedures for randomization of participants that via an electronic database that can be accessed by both sites and will develop a similar set of procedures and remotely accessible databases for data entry at each of the sites. All transmissions will be encrypted and delivered via secure servers.

Dr. Gonzalez (PI) oversees a research lab at the Ferkauf Graduate School of Psychology, Yeshiva University, which is co-located with Einstein. Graduate students in the Clinical Health Psychology PhD program, as well as two post-doctoral fellows under his supervision, have relevant expertise and experience with qualitative interviewing, participant assessment, and data management/analysis. They will be involved in the activities of the proposed study, at PCIP, on an as-needed basis as part of their mentored research experience and training. All trainees who take part in the study will be trained in human subjects research and approved by the Einstein IRB prior to their involvement.

The organizational structure for the proposed project is based on a similar model that has proven effective for the *NYC Care Calls Study*, which enrolled 812 adults with type 2 diabetes from PCIP-affiliated practices. Dr. Gonzalez (PI), Drs. Walker and Schechter (Co-I) have a history of successful collaboration with Ms. Linnell and PCIP on this project and this experience will ensure continued success in the proposed collaborative research.

The Dissemination Plan

As recipients of this award, Drs. Chambers and Gonzalez will ensure the clinical trial it will support is registered and results are submitted to ClinicalTrials.gov according to the timelines and requirements specified in the NIH Policy on the Dissemination of NIH-Funded Clinical Trial Information (NOT-OD- 16-149). We plan to register once the protocol is finalized during the first 6 months of the award, before any participants are enrolled. However, we will ensure that registration will occur no later than 21 days following enrollment of the first subject to adhere to the expectations for NIH-funded clinical trial information. Updates will be made within the required timeframes, no less than once every 12 months, to reflect any material change in the study status and to keep the record current. Results summary and required documents will be submitted within the timeframes specified in the regulation.

Drs. Chambers and Gonzalez will ensure the Informed Consent Forms for all clinical trials under this award include the following FDA specified disclosure statement, exactly as written, notifying subjects that the study will be submitted to ClinicalTrials.Gov: *A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.*

Albert Einstein, has a written internal policy requiring registration and results reporting on ClinicalTrials.gov, in compliance with NIH and FDA requirements. In addition, the internal policy requires timely updates to the study record as required by FDA regulations and NIH policy. To ensure compliance with NIH's registration deadline, the Institutional Review Board (IRB) requires the registration NCT# before the study protocol can receive IRB approval. To enable compliance with all ClinicalTrials.gov reporting requirements, Albert Einstein sends notifications on activities required to keep the study record current and provides personnel, training, and any additional resources needed.

Beyond adhering to these requirements related to ClinicalTrials.gov, we will disseminate our results more broadly, through presentations at national professional and scientific conferences, and in peer- reviewed journal publications, with open access publishing whenever possible. We will also make information about these publications available on our website for the New York Regional Center for Diabetes Translation Research (www.newyorkregionalcdtr.org), one of 8 Centers funded by NIDDK to promote translational research for diabetes prevention and control. We will also disseminate announcements for the publications among the members of our NY-CDTR, working in diabetes prevention and control in the NY-region. We will also reach investigators across the country focused on Latino populations, through our Latino Network for Diabetes Translation Research, a National Resource Core of the NY-CDTR. In total our membership list will reach 90+ investigators across the country. NIDDK also provides a mechanism to share preliminary findings and resulting publications with the other 7 funded CDTRs through a CDTR Directors monthly telephone meeting and a yearly in person meeting that features an e-book highlighting each CDTR's most important publications. Thus, our dissemination will penetrate into the memberships of CDTRs across the country focused on diabetes translation research. The intervention protocol will be made available on the NY-CDTR website and will be submitted to the CDC for distribution as a recognized program.

Our partnership with Ms. Jill Linnell at the Primary Care Information Project/NYC-Department of Health and Mental Hygiene provides an avenue of local dissemination. Our partner is committed to support the adoption and maintenance of *Power-Up* as a men-focused diabetes prevention program if it is proven to be effective and if costs are demonstrated to be reasonable and in a favorable balance with program benefits by the current study. Through this healthcare system, *Power-Up* could be disseminated to thousands of men obtaining care in diverse healthcare system settings across New York City.

sIRB Communication Plan

The Einstein IRB (Einstein) will be serving as the Single IRB (sIRB) in this proposed multi-site study involving human subjects' research. As the sIRB, Einstein will fulfill the requirements set out in 45 CFR Part 46, and 21 CFR Parts 50, 56, 312, 600, 812, as applicable, by conducting initial and continuing reviews of protocols for all participating domestic sites, including amendments, unanticipated problems, protocol deviations, and required reporting to federal oversight agencies. The sIRB will also serve as the Privacy Board, as applicable, to fulfill the requirements of the HIPAA Privacy Rule for use or disclosure of protected health information for research purposes.

The participating sites identified in the Project/Performance Site Locations section of this proposal have indicated their willingness to rely on Einstein as the selected sIRB and the PIs have obtained documentation of their agreement via letter. In turn, the Einstein IRB has provided a Letter of Support indicating its commitment to serve as the sIRB.

At the time of award, Einstein sIRB representatives will meet with the PIs and Research Study Team to review their responsibilities, as outlined in the relevant Reliance/Authorization Agreements (AA), and to review Einstein's sIRB Policies. It may be determined during this meeting that the use of the Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB Reliance platform, funded by the National Center for Advancing Translational Sciences (NCATS), is the most efficient model for implementing the authorization agreements among the participating sites.

Prior to the signing of AAs between Einstein and the participating sites, the sIRB will work with the PI and Research Study Team to ensure that the AA is signed by both institutions. The PIs will communicate the terms of the agreements with each participating site. AAs will be considered fully executed once signed by the Institutional Officials at both Lead and Relying Sites.

As outlined in the AAs, the relying institutions will be expected to contact the Lead PI when there are study events, required reports, and other significant issues that must be reported to the sIRB. The Lead PI will communicate with the sIRB for guidance. The sIRB will offer, as needed, to communicate directly with the relying sites to resolve issues.

The PIs will obtain prior approval from NIH to request additional sites to the study. If approved, the PIs will coordinate with the participating site to obtain a signed AA. The same processes as described above will apply.

The Einstein IRB Office will maintain the signed Authorization Agreements and will provide copies to the relying sites.