PARTNERS HUMAN RESEARCH COMMITTEE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR

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PROTOCOL TITLE

PREMIER: PREvention of Metabolic Illness through prEcision nutRition

FUNDING

Pilot and Feasibility Award program from the Nutrition Obesity Research Center at Harvard (NORCH)

VERSION DATE

08/15/2023

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SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

The proposed study will examine interpersonal post-prandial responses to specific foods and meals based on personal features and characterize their variability across study groups. We propose to conduct a recall-by-genotype study among individuals with extremes genotypes influencing dietary intake from the Partners Healthcare Biobank to study the glycemic and metabolomic responses to a standardized and an election meal in a full-day clinic visit.

The specific objective of the PREMIER study is to carry out an interventional dietary study to measure the response of blood glucose and other biomarkers to a standardized meal or an election meal of varying nutritional content.

The specific hypothesis of this study is that deep molecular, physiological, and behavioral profiling can identify mechanisms underlying variable responses to specific foods and meals. The study will deliver preliminary data to link underlying genetic influences for food preferences with variable metabolic responses to different types of meals. If successful, it is foreseen that this data could be used to inform personalized dietary interventions focused on optimizing substrate metabolism and body weight.

BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

Dietary intake is a major driving force behind the escalating obesity and type 2 diabetes (T2D) epidemics and is shaped by the confluence of social and environmental factors acting on a background of inherited biological differences (Atasoy et al., 2012; Rankinen and Bouchard, 2006; Swinburn et al., 2011; van der Klaauw and Farooqi, 2015). To inform more effective obesity and T2D prevention strategies, it is crucial to better understand the biological, environmental, and social factors that influence how people interact and respond to specific foods (Cefalu et al., 2015; Hawkes et al., 2015; Unwin et al., 2010; White, 2016).

In a recent large-scale genome-wide association study, our research team has identified 96 genomic regions associated with overall variation in dietary intake (Merino et al., 2019). These findings provided insight into specific brain regions, cell types, and neural processes regulating food intake and intermediary metabolism. However, the clinical utility of this information remains largely unknown. Two recent advances in the genetics of complex traits could offer translational opportunities. First, the development of modern computational methods to cluster genetic variants based on underlying similarities, and collapsing them into cluster-specific polygenic scores (PSs), represents an efficient approach to capture genetic susceptibility and has the potential to deliver clinical benefit through enhanced capacity to maximize response to tailored behavioral interventions for the prevention and management of obesity and T2D (Udler et al., 2018; Udler et al., 2019). Second, the advent of recall-by-genotype studies, an approach to recall participants from clinical studies based on their specific genotype, can be used to identify people with the desired genotypes for clinical interventions and deep phenotyping (Corbin et al., 2018).

Connecting knowledge about human genetic variants with information from circulating metabolites can be particularly useful in understanding the mechanisms by which some people experience a detrimental response to specific foods. Large clinical trials have shown that close adherence to healthy lifestyle interventions can prevent or delay the progression to T2D by ~50% (Knowler et al., 2002; Pan et al., 1997; Ramachandran et al., 2006; Tuomilehto et al., 2001). However, large variability exists in response to dietary interventions (Korem et al., 2017; PW; Spector; Zeevi et al., 2015). Understanding the links between food intake signaling mechanisms and intermediate metabolism may help optimize the beneficial impact of dietary interventions and strengthen adherence to personalized dietary recommendations.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

We will recruit 30 healthy adults, 21-65 years of age for this study. Participants will be recruited from the Partners Healthcare Biobank, an electronic health records biorepository with clinical

and genetic data from ~36,000 individuals, who have consented to re-contact and through Patient Research Invitation (PRI). Participants will be excluded if they:

- Refuse or are unable to give informed consent to participate in the study.
- Have type I or type II diabetes mellitus or are taking medications for type II diabetes mellitus. Those not on medications but having a capillary glucose level of >126 mg/dL based on fingertip glucose measurements will be excluded.
- Are obese (BMI>30.0kg/m^2) or underweight (BMI≤18.5kg/m^2).
- Have had a heart attack (myocardial infarction) or stroke in the last 3 years.
- Have had cancer in the last 3 years, excluding skin cancer.
- Have an ongoing inflammatory disease i.e. Rheumatoid arthritis, systemic lupus erythematosus, polymyalgia and other connective tissue diseases.
- History of cirrhosis and/or aspartate aminotransferase (AST) or alanine aminotransferase (ALT) more than 3 times the upper limit of normal (ULN).
- No known sickle cell disease or anemia.
- Are currently suffering from acute clinically diagnosed depression.
- Currently taking or intending to take during the study duration any medication known to affect glycemic parameters, such as glucocorticoids or fluoroquinolones.
- Are unable to fast from 9pm the night before the clinic visit until 9am on the clinic day
- Are pregnant or breastfeeding.
- Are participating in another clinical study.
- Are vegan, suffering from an eating disorder or unwilling to eat foods that are part of the study.

Briefly describe study procedures. Include any local site restrictions, for example, "Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

Eligible participants who have reconsented to contact from the Partners HealthCare Biobank with desired genotypes and through Patient Research Invitation (PRI) will be contacted by study coordinators via our IRB approved contact letter.

Eligible participants will then be invited to attend the Translational and Clinical Research Center at MGH for their visit. Before the visit, participants will be sent pre-visit instructions, questionnaires and consent forms. Informed consent will be taken at the visit. After participants have given informed consent to take part they will have a fasting blood sample taken. In the event that a participant does not provide informed consent, no samples will be collected from the participants. Participants will then undergo a brief medical examination to measure BP, waist circumference, weight and height. During the clinical visit, participants will be cannulated, consume a set breakfast and an election lunch and provide blood samples at 9 time points (at baseline, [Breakfast meal], 30, 60, 120, 180, 240, [Lunch meal], 270, 300, 360 minutes (all minute intervals are relative to their first bite of the breakfast test meal)).

The subjects will also be asked to collect a stool sample the day of the visit or within 48 hours. In the event that a participant cannot produce a stool specimen during the visit, arrangements will be made to have the stool sample returned by mail. The participant will be given a stool collection kit containing illustrated instructions and all materials required to collect the stool specimen. The stool specimens will be collected into preservative-containing specimen tubes

using standard Human Microbiome Project protocols. There are no discernible risks associated with stool collection.

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

N/A

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

This study has been designed to reduce participant burden as much as possible while allowing for the robust data/specimen collection necessary to obtain predictive measures of dietary responses. All clinical procedures are routine and carry minimal risk, but are voluntary and participants can withdraw consent at any time.

The risks associated with collecting blood anthropometrics and questionnaires, present minimal risks. Total blood volume is 134ml at the point it reaches the lab, and a total of 170 ml taken from participant. As this is below 300ml over at least 6 hours, this does not result in added risk. Normal blood donation volume is 450-500ml. If nursing staff have any reason to be concerned with this volume of blood draw for any individual participant then they will discharge the participant. A total of 170 ml is calculated as 134ml for sampling, plus up to 36 mL discarded when removing flush from the cannula (4mls at each blood draw except at baseline to remove the flush so 4mlx9=36ml). Randomized study IDs will be assigned to participants to protect the patients' sensitive health information. Since these patients are healthy no adverse events are anticipated, however given that there is a dietary intervention involved participants will be monitored closely by study staff for possible adverse events during the visit day.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

Participants can withdraw their consent at any time during the course of the study without giving any reason by contacting the study contact number. Similarly, the participant can withdraw their consent for the continued retention and use of their samples even after they have been collected, without giving a reason. Reason for discontinuation from the study will be asked about sensitively and recorded.

If a subject withdraws consent to the use of donated biological samples, any retained samples will be disposed of/destroyed. If these samples have already been used for data analysis (e.g. sequencing or metabolite measurement) it will not be possible to destroy this data and it will remain as a part of the study, but any data that is retained will be anonymized.

The Principal Investigator:

- Will ensure subjects' withdrawal of informed consent is recorded. Will ensure that biological samples from that subject, if stored at the study site, are immediately identified, disposed of/destroyed and the action documented.

- Will ensure that the laboratory(ies) holding the samples is/are informed about the withdrawn consent immediately and that samples are disposed of/destroyed and the action documented.

All participants must consume the baseline breakfast and provide baseline fasting bloods. Failure to meet these two requirements will result in termination of continued study participation as other endpoints will be unevaluable. If any other sample collections, dietary interventions, or blood timepoints are missed or unable to be completed, the subjects may continue with participation and these missing items will be logged by the study staff.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

The risks associated with collecting blood, anthropometrics and questionnaires, present minimal risks. Potential risks and discomforts include phlebotomy, stress from abnormal laboratory values, and loss of confidentiality.

Drawing blood involves minor risks and discomforts including brief pain and possibly a bruise at the needle/cannulation site. Occasionally, a person may feel faint when their blood is drawn. Infections rarely develop and are treatable.

Some participants in this study will carry genetic risk and clinical factors for diabetes and it is therefore possible that some will have undiagnosed pre-diabetes or diabetes; some may have other unrecognized conditions that may come to attention through routine blood work during this study. Participants with laboratory values deemed by the study physicians to be clinically actionable will be informed by phone and letter and asked to follow up with their primary care physician, who may also be notified if the participant agrees. Physician's phone and email will be listed on the letter so the subject can reach out to us if they have any questions about their results.

Randomized study IDs will be assigned to participants to protect the patients' sensitive health information, however there could be a breach in confidentiality involving protected health information, and the information collected from taking part in a genetic study could influence insurance companies or employers regarding a patient's health. The privacy of all subjects will be protected and confidentiality maintained.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects." Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

There is no specific individual health benefit expected as a direct result of participating in this study. However, participants will be provided information about the laboratory results of their individual participation in the research study. We will provide lab results from the visit day that include glucose and insulin levels, kidney and liver function test, and lipid panel results that we will measure. The research we are doing is only a stepping stone in understanding metabolic responses to foods. Most of the findings that come from the study will not be relevant to personal health. These studies will help advance our clinical and scientific understanding of how metabolic processes in the body are influenced by diet and our microbiome and ultimately how these processes may contribute to factors influencing human health and disease.

Participants will be remunerated for their time (US $70) following successful completion of the study. The remuneration will be in the form of general use, credit-card style (e.g. American Express or Visa) pre-loaded gift cards. Participants will receive two free meals during the study visit. They will also receive a voucher for your transportation to the study visit, which will cover the cost of parking or 2 passes on the MBTA.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

Both men and women and persons of all races and ethnicities will be included. Pregnant women and those six months after giving birth or still breastfeeding will be excluded due to the potential for confounding on biomarkers/metabolites for dietary prediction models.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

The nature of the recruitment and study procedures will require continuous and unscheduled patient interactions and the limitations of our study staff in speaking languages other than English preclude us from enrolling non-English speaking participants at this time.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English

https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Non-English-Speaking-Subjects.pdf

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

The Partners HealthCare Biobank is a large research data and sample repository working within the framework of Partners Personalized Medicine. It provides Partners investigators with required approval from the Partners Institutional Review board (IRB) access to high quality, consented samples linked to clinical data stored, some additional health information and survey data, and genomic data. Participants will be contacted via a contact letter, and an opt-in/opt-out card. The first recruitment efforts will be with individuals who have given permission for re-contact from the Partners HealthCare Biobank. We plan to recruit all required individuals from those who participated in the biorepository.

Patient Research Invitation (PRI): RPDR will be used to pre-select MGB patients who have not yet opted-out from PRI, enrolled in Partners Biobank, between the ages of 18-79. We will first perform chart reviews and RPDR queries to screen for potentially eligible subjects using the inclusion and exclusion criteria for this study. Eligible potential subjects will then be contacted directly by researcher about the study via Patient Gateway message or letter or announcement. The patient gateway message/letter or announcement will explain the study in simple terms and include contact information (i.e. phone number and email for study team), so that the patients can choose to "opt-out". If the potential research subject has not declined further contact within 7 days of the Patient Gateway message and/or letter, the research coordinator will contact the patient via telephone to determine their interest in participating in the study and confirm their eligibility using a screening form based on the inclusion and exclusion criteria. The research coordinator will send further information and an informed consent form via mail or email to eligible participants, inviting them to come to the first visit.

The individuals who opt-in will be screened over the phone by the study team (see Call Script #1). Individuals who do not return the card will be called by the study team to gauge interest and, if interested, screened over the phone by the study team. Individuals who opt-out or who indicate they are not interested during the phone call will not be contacted further regarding this study. Potential participants who wish to participate in the study and meet no exclusion criteria will be mailed instructions for the first visit, and a copy of the consent form with encouragement for review prior to the first study visit. Any interim questions regarding the protocol will be answered over the phone. After reading the study protocol and consent form, potential participants who still wish to participate will be invited to attend the Visit.

If the patient contacts the study coordinator by phone, the study coordinator will outline the study using a call script and assess eligibility (inclusion criteria) and minor exclusion criteria (e.g. pregnancy, food allergies to dietary components; see questionnaire script) and answer any

questions the patient may have. Additionally, if the patient does not contact the study coordinator within 2 weeks of sending the letter, they will be contacted by phone and the study will be outlined. If the patient indicates that they do not wish to learn more about the study, they will not be contacted further. If it becomes apparent during our recruitment that women or minorities are underrepresented, focused effort will be made to recruit additional members of these groups according to the demographics of the greater Boston area.

If the participants are still interested and have met the initial screen, they will undergo a more detailed eligibility assessment performed by a study coordinator over the phone (see script). At this point the participants will be given an informational booklet, the Participant Information Sheet (PIS), and consent form, electronically or sent via mail, that fully describes the study. This booklet will assist in the informed consent process. If individuals remain interested in participating, the participants will be invited and scheduled to attend their clinical day at which time they will sign the informed consent.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

Participants will be remunerated for their time (US $70) following successful completion of the study. The remuneration will be in the form of general use, credit-card style (e.g. American Express or Visa) pre-loaded gift cards.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Recruitment-Of-Research-Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Guidelines-for-Advertisements.pdf

Remuneration for Research Subjects
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Remuneration-for-Research-Subjects.pdf

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

Interested participants will be sent an information sheet (see Participant Information Sheet and Pre-visit instructions) and informed consent form by mail or by email, at least 2 weeks before their baseline visit is scheduled. At the baseline visit or the day before the first visit (if consenting remotely), it will be the responsibility of the researcher to obtain written (signed and dated by the participant and researcher) informed consent from each individual participating in the study after adequate explanation of the aims, methods, objectives, benefits and potential risks of the study. The researcher will also discuss the procedures that will happen as part of the study prior to consent taking and if the volunteers are willing, the relevant box on the consent form will be ticked. The researcher will also explain to the participants that they are completely free to refuse to enter the study or to withdraw from it at any time without obligation to give a reason. Participants will have the opportunity to ask questions before they sign the consent form. The participant will be provided with a copy of their signed and dated consent form and any other written information which they should be instructed to retain.

In the event that a potential participant is known to one of the study investigators, (for example a work colleague or personal acquaintance) the study team will ensure that the informed consent procedures will be conducted by an alternative investigator who has no relationship with the volunteer.

Consent will be taken by the designated trained researchers responsible for conducting the study and experienced in patient communication and consent taking. All potential participants will have been given the informed consent document and will have had adequate time to read it, understand the protocol, the risks and burdens and benefits, and will have had time to ask questions. The researchers will reiterate this information in person prior to taking consent. Only participants who have capacity to provide consent for themselves will be recruited.

It is essential that participants fully understand the requirements of the study and therefore participants without a good understanding of verbal or written English will not be included in the study as there is not the provision for translation or interpreters.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Partners policy:
Informed Consent of Research Subjects:
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Informed-Consent-of-Research-Subjects.pdf

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the

planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

We do not anticipate safety issues since this study does not include a therapeutic intervention, beyond the risks outlined above for blood draws. The principal investigator will monitor data quality and integrity, review subject enrollment, and address any subject-related issues that might arise. It will be the discretion of the principal investigator and the sponsor to determine whether the research should be altered or stopped.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

As this study is a dietary intervention study, safety monitoring will focus on unanticipated events involving risks to participants, including unanticipated problems that meet the definition of a serious adverse event.

Adverse event (AE): any untoward medical occurrence in a patient or study subject
Serious adverse event (SAE): any untoward and unexpected medical occurrence or event that:

1. Result in death
2. Is life threatening
3. Requires hospitalization or prolongation of existing in-patient hospitalization
4. Results in persistent or significant disability or incapacity

Medical judgement will be exercised in deciding whether an AE is serious. Important AEs that are not immediately life-threatening or do not result in death or hospitalization but may jeopardize the subject or may require intervention to prevent one of the other outcomes listed in the definition above will also be considered serious.

Adverse events will be recorded and reported to the Principal Investigator. The event will also be documented and discussed with all members of the research group in the research departmental meetings and with the sponsor.

All SAEs (both related and unrelated) will be recorded and reported immediately to the Principal Investigator and the sponsor. Relapse and death due to an unrelated or pre-existing condition, and hospitalization for treatment of a pre-existing condition do not require reporting as SAEs. All SAEs should be reported to the research ethics committee within 15 days of the Principal Investigator becoming aware where in the opinion of the Principal Investigator, the event was:

1. Related i.e. resulted from administration of any of the research procedures
2. Unexpected i.e. an event that is not listed in the protocol as an expected occurrence

Although no formal adverse event reporting will take part in this study, any significant events relating to the procedures surrounding this study that the Investigator feels are important, will be documented as a Serious Adverse Event (SAE). Details of the SAE will then be kept in the Investigator site file and the Study Master File and notified to the IRB and sponsors as appropriate.

The principal investigator will be reviewing each subject's data periodically throughout the duration of the study for quality, validity and integrity assurance and for adherence to the IRB approved protocol. In addition, the study coordinators will monitor subject documents on an ongoing basis. All source data will be organized and filed into subject binders. Any pertinent notes to file regarding the subject will be documented by the study coordinator and kept in the applicable subject binder. All subjects will be assigned a study identification number. In addition, interim and final data and safety monitoring reports performed twice during the study (at 1/3 and 2/3rds enrollment) by the principal investigator will include the following:

- Changes to protocol including
    - Amendments to the protocol
    - Investigator/key personnel changes
    - Changes to the consent document and communications to participants regarding changes
- Cumulative adverse event summary
    - Review and analysis of adverse events
    - A summary of any other safety issues

- Monitoring the progress of the study
- Narrative summary of interim or final data analyses
- Protocol adherence
    - Protocol violations
    - Protocol deviations
- Recruitment and retention summaries
    - Enrollment numbers
    - Withdrawals (provide summary of reason(s) for withdrawal)
    - Dropouts (provide summary of reason(s) for dropouts)

For guidance, refer to the following Partners policies:

Data and Safety Monitoring Plans and Quality Assurance
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/DSMP-in-Human-Subjects-Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://www.partners.org/Assets/Documents/Medical-Research/Clinical-Research/Reporting-Unanticipated-Problems-including-Adverse-Events.pdf

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

Personal information along with study data will be kept in REDCap, an online Partners approved data storage site or using an electronic clinical research form Microsoft Access database that is stored locally. Only study coordinators and Investigators will have access to this information. The In-study engagement team that interacts with participants during the study will have access to a participant's name, phone number, and email address for the purposes of interacting with the participant, answering their questions and troubleshooting issues. However, any and all data stored at the completion of the study will be void of any personal health identifiers and only labelled with their study ID numbers. Only investigators and study staff will have access to the data stored in password protected computer databases. All laboratory samples will be labeled with a unique, non-identifying label.

We may send deidentified samples to a third party, such as the Broad Institute or other suppliers for analysis. These specimens will not be linked to any individual identifiers associated with the patients. For sending deidentified samples to third party, we will generate a contract for this purpose through hospital supply chain.

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

Deidentified study data may be shared with our direct collaborators at the Broad Institute who will profile samples for metabolomics studies. We may collaborate with investigators at the Harvard T.H. Chan School of Public Health, or other instates for research purposes, laboratory assays, or analysis. Any biospecimens sent to collaborators, including blood, serum or stool samples for laboratory measurements or analysis will not be linked to any individual identifiers associated with the patients. Similarly, any data sent to collaborators for research purposes will be de-identified. Any additional collaborators outside Partners will be added through amendment of this protocol. We will obtain letter of agreement between academic collaborators prior to transfer of samples.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

All specimens and data will be stored and maintained in the laboratory of Dr. Jose C. Florez (Co-Investigator) at MGH

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

Data derived from eternal collaborators on specimens curated as part of this study, specifically from the Broad Institute or other suppliers for analysis, will be shared as agreed upon in the contracts negotiated with Partners.