PROTOCOL TITLE
Mindfulness-Based Cognitive Therapy Delivered via Group Videoconferencing for Acute Coronary Syndrome Patients with Elevated Depression Symptoms

VERSION DATE
November 6, 2018

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

Elyse Park, PhD

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Mindfulness-Based Cognitive Therapy Delivered via Group Videoconferencing for Acute Coronary Syndrome Patients with Elevated Depression Symptoms

FUNDING

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VERSION DATE

11.6.18

SPECIFIC AIMS

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

Specific Aim #1 (Qualitative research): To identify ACS patients' specific needs and preferences for depression treatment via in-person focus groups (N=8 groups [approximately 8 per group]) to (a) guide MBCT adaptation; and identify barriers and facilitators to (b) group videoconferencing delivery, and (c) blood spot data collection to enhance feasibility.

Hypothesis: Participants will report specific physical, cognitive, and behavioral symptoms to be targeted in the intervention, discuss barriers and facilitators to participating in a videoconference treatment program and completing blood spot data collection procedures.

BACKGROUND AND SIGNIFICANCE

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

It is critical to treat depression in patients with acute coronary syndrome (ACS). Among the one million ACS patients in the U.S. each year (e.g., myocardial infarction, unstable angina), 15-20% meet criteria for major depressive disorder and up to 45% have elevated depression symptoms, rates 3x higher than the general population. Meta-analyses of over 4,000 ACS patients and 53 studies have found that depression is an independent risk factor for recurrent cardiac events, re-hospitalizations, cardiac mortality, and all-cause mortality, beyond other traditional risk factors. Left untreated, depression persists for years and doubles the risk of death through biological and behavioral mechanisms. Biologically, depression causes inflammation through neuroendocrine alterations, leading to atherosclerotic plaque formation and rupture. Behaviorally, ACS patients need to make multiple lifestyle changes, but depression symptoms (e.g., disinterest, lack of motivation) prevent engagement in cardiac health behaviors (e.g., physical activity, diet). Thus, depression treatment is necessary to promote biological and behavioral changes important for survival.

Depression treatments for ACS patients need improvement. More ACS patients prefer psychological (75%) rather than pharmacological depression treatments (20%). However, the recommended psychological intervention, cognitive-behavioral therapy (CBT), has limited effects on depression and cardiac outcomes. Targeting the mechanisms that link depression to ACS could improve treatment

efficacy, but CBT does not aim to target a key mechanism, i.e., inflammation. Consistent evidence from multiple meta-analyses suggests that depression is associated with elevated levels of inflammatory cytokines, particularly C-reactive protein (CRP), interleukin-6 (IL-6), and TNF-α. These same specific cytokines are also elevated, positively correlated with depression symptoms, and independently increase the risk of mortality in patients with cardiac disease. Of note for depression treatment, the relationships are bidirectional: treating depression reduces inflammation, but reducing inflammation also reduces depression symptoms, making CRP, IL-6, and TNF-α salient treatment targets for both depression and cardiac health in ACS patients.

Mindfulness-Based Cognitive Therapy (MBCT) could improve depression and cardiac health for ACS patients. MBCT is an 8-week manualized group intervention that combines CBT with mindfulness meditation to treat depression; it is as effective as antidepressant medication for relapse prevention and reduces symptoms in active depression. The American Heart Association (AHA) recently highlighted the potential benefits of meditation for cardiac health and the need for further research in this area. Indeed, through the addition of mindfulness training, MBCT could improve both depression and cardiac health. First, mindfulness meditation can reduce levels of CRP, IL-6, and TNF-α, which reduces depression symptoms and benefits cardiac health. Second, meditation increases pro-sociality (e.g., compassion, altruism) and social support, both of which reduce depression symptoms. Given that social isolation is an independent risk factor for ACS mortality and pro-sociality improves cardiovascular functioning, social improvements could have direct benefits on cardiac health. Next, MBCT improves emotion regulation (e.g., rumination about a recurrent event, acceptance of lifestyle changes), which is a key treatment target for depression. Lastly, mindfulness training improves cardiac health behaviors, likely by improving emotional outcomes. Improvements in depression also lead to further improvements in inflammation and pro-sociality to further promote cardiac health.

Research supports the feasibility of MBCT for depression treatment in ACS patients. Two meta-analyses (18 trials) have demonstrated that mindfulness interventions are feasible, acceptable, and reduce depression symptoms in patients with cardiovascular disease (d = .35 - .61). ACS patients are similar to other cardiac disease patients (e.g., age, comorbidities) and thus are also likely to find mindfulness interventions acceptable. In fact, ACS patients may be most interested in depression treatment because they are motivated to improve their health following the acute cardiac event. Most research in patients with cardiovascular disease has used Mindfulness-Based Stress Reduction (MBSR), which is very similar to MBCT, but does not incorporate a CBT approach to target depression specifically. MBCT shows larger effect sizes for depression than MBSR and thus might be particularly useful for ACS depression treatment.

An electronic health (e-health) approach is needed to improve treatment outreach. Most ACS patients prefer behavioral depression treatments, but these are burdensome, not widely accessible, and present barriers. In a study of nearly 700 primary care patients, 78% of those with depression reported logistical and emotional/physical barriers to accessing treatment. E-health technologies can overcome these barriers to reach more patients and effectively treat depression. In a study of over 200 patients with cardiovascular disease, 85% had internet access and 74% of them preferred e-health interventions. ACS patients tend to be older adults ($\geq$65 years), the fastest growing group of computer and internet users, who report positive experiences with technology used at home. A systematic review of 54 trials found that e-health interventions are feasible for older adults with medical problems, including those with cardiovascular disease.

It is feasible to deliver MBCT via e-health technologies. E-health mindfulness interventions are feasible and can improve health outcomes in patients with medical problems. However, research has focused on websites that patients use independently, which does not allow for synchronous contact with a clinician or peers, leading to a smaller treatment effect and increased attrition, and eliminating the health benefits of social support. Group videoconferencing combines accessibility with synchronous contact, shows comparable efficacy with in-person treatments, and is a validated approach to behavioral

intervention delivery. Two studies demonstrated the feasibility of videoconferencing to deliver mindfulness interventions to patients at their own home. Thus, group videoconferencing is a promising but underutilized approach to MBCT delivery.

MBCT via group videoconferencing is likely to be attractive and feasible for ACS patients. Web-based mindfulness interventions are feasible and reduce depression symptoms in patients with cardiovascular disease and other older adult populations. The AHA has emphasized that a benefit of meditation for cardiac health is the possibility of online delivery, but no research has applied MBCT via group videoconferencing to ACS patients with elevated depression symptoms.

This proposal is to develop an MBCT intervention adapted for ACS patients and ultimately test the feasibility and acceptability of the intervention, delivered via group videoconferencing, for ACS patients with elevated depression symptoms in a pilot randomized controlled trial (RCT). This research will incorporate a novel, minimally invasive blood spot data collection procedure to measure inflammation in a future RCT. Toward these goals, the purpose of the current study is to collect qualitative data on ACS patients' treatment needs, to inform MBCT adaptation, and to explore the barriers and facilitators for using online videoconferencing and providing dried blood spot samples, to promote feasibility of these procedures in the future RCT.

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."

This qualitative research study will involve approximately eight in-person focus group of ACS patients (approximately 8 participants per group, stratified by gender and ACS; total N = approximately 70) to explore patients' treatment needs and preferences for an adapted MBCT intervention, and barriers and facilitators for future intervention research procedures (i.e., videoconferencing delivery of the intervention and collection of dried blood spots).

Inclusion criteria:
1. Lifetime ACS per medical record and patient confirmation
2. Current elevated depression symptoms (PHQ-9$\geq$10)
3. Age 35-85 years
4. Access to high-speed internet

Exclusion criteria:
1. Active suicidal ideation or past-year psychiatric hospitalization
2. Non-English-speaking
3. Cognitive impairments preventing informed consent.

There are no exclusion criteria with respect to ethnicity or socioeconomic status.

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.

Summary of Methods: Participants will be recruited for a qualitative research study involving participation in a focus group to explore ACS patients' preferences and barriers/facilitators for an adapted

MBCT videoconferencing intervention and completion of dried blood spot research procedures. Focus groups will be conducted in person. Four focus groups are planned but further would be conducted as needed until thematic saturation is reached. Participants will receive $30 remuneration for their participation.

Recruitment. Participants will be identified using the MGH Research Patient Data Registry (RPDR). IRB approval will be obtained to search the RPDR for patients who meet eligibility criteria, including both RODY and non-RODY patients (Research Options Direct to You; i.e., patients who have agreed to be contacted directly about research studies). Non-RODY patients will be sent an opt-out letter from our team and their cardiologist. RODY patients will be sent an opt-out letter by the study team. Patients who do not opt-out within two weeks will be contacted by phone and screened for eligibility. The RA will contact all participants by phone that do not opt out within 2 weeks. The RA will explain the study procedures, answer any questions, and complete eligibility screening by administering the PHQ-9 to assess current depression symptoms, and by asking about past-year psychiatric hospitalizations that may not be in the electronic medical record, and access to a computer with high-speed internet or a smart phone. The RA will also review potentially eligible participants' medical records to confirm eligibility as needed (e.g., if ACS history is unclear). If participants meet study criteria, they will complete the verbal consent process described below.

Baseline data: Medical information about enrolled participants will be obtained from the patients, care providers, and/or the electronic medical record as required for characterization of our population. This information will include data about medical data related to ACS (e.g., date of ACS, type of ACS, ACS treatments procedures and medications) and sociodemographic data (age, gender, race/ethnicity, education, and marital status). This information will help to ensure that the population we recruit is a representative population of patients living with ACS so that the interview information gathered to inform the MBCT intervention is applicable to the broadest population of patients.

Focus groups: A semi-structured interview guide will be developed to conduct approximately eight in-person focus stratified by gender and time since ACS, with 2 groups for each strata (i.e., 2 groups of women $\leq$2years ACS, 2 groups of women > 2 years ACS, 2 groups of men $\leq$ 2 years ACS, 2 groups of men > 2years ACS). Each focus group will last approximately 90 minutes each. Focus groups will focus on exploring (a) changes after ACS, such as psychosocial changes and health behavior changes; (b) specific preferences for the MBCT intervention; and (c) potential barriers and facilitators of group videoconferencing and (d) blood spot data collection. The interview guide will be piloted with 3-4 participants and refinements will be made as needed before conducting the focus groups. Focus groups will be conducted until thematic saturation is reached. Focus groups will be audio-recorded for transcription and data analysis. The results will be used to guide MBCT adaptations and research procedures for future clinical trials.

The focus groups will be generally organized as follows (see Interview Script): first, participants will be asked to discuss changes they've experienced after an ACS, including psychosocial and behavioral changes. Next, participants will be asked about their thoughts on a treatment program to help manage distress, including their general interest in participating and their preferences for the format and timing of the program. Next, participants will be asked about potential barriers and facilitators to using group videoconferencing for the intervention, including the types of training and assistance they would want in order to use this technology comfortably. Lastly, participants will be provided information about blood spot data collection techniques and asked about barriers and facilitators to providing dried blood spots, with questions including topics such as privacy and logistics. Participants will also be asked what type of training or other assurances they would want in order to feel comfortable providing dried blood spots. Throughout the focus group, questions will be framed as open-ended questions as appropriate.

Measurement of health outcomes. Depression symptoms, trait mindfulness, health behaviors, and other psychological, behavioral, and physical constructs that may potentially be impacted by the MBCT

intervention in subsequent trials will be measured. Doing so in this study will allow for an evaluation of the feasibility using of these scales in this specific patient population. The measures that will be included are all previously validated and show appropriate psychometric properties. The measures are: Five Factor Mindfulness Questionnaire- 15 item (FFMQ-15), Perceived Stress Scale-4 (PSS-4), Difficulties in Emotion Regulation Scale (DERS), Positive Affect Negative Affect Schedule (PANAS), Rumination Response Scale (RRS), Inclusion of Other in Self Scale (SOFI), Interpersonal Reactivity Index (IRI), Dispositional Positive Emotions Scale- Compassion (DPES-C), Medical Outcomes Study – Specific Adherence Scale (MOS- SAS), PROMIS- Physical Function, PHQ-9, and SF-12.

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.

The risks to participants in this study should be relatively limited. Patients may experience discomfort from discussing psychological experiences and could experience the evaluation as intrusive. Participants who do not find the study to provide a benefit to them may find this upsetting as well. All measures possible will be taken to ensure patient comfort and participants will be informed that they could exit the focus group at any point with no penalty. The PI or other psychiatrist/psychologist study staff will be available while focus groups are being conducted to intervene if needed (due to patient discomfort or to answer specific questions about the study). Participants will also be informed that they can choose not to complete any surveys or answer any specific survey items that make them feel uncomfortable.

As with any study, there is the risk of a breach of confidentiality; these risks will be minimized by using participant ID numbers rather than identifying personal data on study documents, and by using locked cabinets/offices and password-protected databases to store personal information. Only study staff (the PI and the research assistant entering data) will have any access to personally identifiable information about participants, and such access will be limited only to information necessary to complete study tasks. Furthermore, the audiotaped recordings of the focus groups will be identified only with an study focus group number (with this number linked to identifying information that is kept in a password-protected database), will be stored in a password-protected folder on Partners' secure network, and will be destroyed once the time period for keeping research-related data has passed. While it is not possible to ensure confidentiality from individual members of the focus group, the focus groups will begin by establishing the requirements and expectations for confidentiality, informing participants of the importance of not sharing details of the focus group, and any identify information about other members of the focus group, with others outside of the group.

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.

This study is a one-time focus group interview lasting approximately 90 minutes. The main psychosocial safety concern related to patients in this study is suicidal ideation, since participants will be ACS patients

with elevated depression symptoms. Subject safety regarding suicidal ideation will be ensured in several ways.

First, eligibility criteria require that patients do not have active suicidal ideation at the time of enrollment, and that they have not been hospitalized for a psychiatric reason in the past year. Thus, it is not likely that participants will report suicidal ideation during the focus group. During the eligibility screening procedures, participants will be administered the Patient Health Questionnaire-9 (PH-9) over the phone. If any patient during phone screening endorses suicidality (i.e., PHQ-9 item 9 score above 0; "Over the past two weeks, how often have you been bothered by thoughts that you were better off dead or of hurting yourself in some way"), the RA will follow our standardized, published specific safety assessment protocol that our team has developed and used in prior funded studies of ACS patients with elevated depression symptoms. The protocol involves further assessing safety risk through a series of structured questions, with specific instructions at each step based on the patients' response. It will begin by clarifying the response to PHQ-9 item 9 (i.e., determining passive versus active suicidality). If patients endorse active suicidality, the RA will further assess safety risk (e.g., plan, intent, past suicide attempts). The RA will notify the PI (a licensed clinical psychologist), and patient's treatment providers about any active suicidal ideation. The licensed psychologist will be immediately paged to conduct further assessment and intervention with patients found to be at imminent risk. The licensed psychologist will inform the patient's primary treatment providers of the patient's symptoms, and assist with the obtainment of further evaluation and care as needed (e.g., through referral to outpatient treatment or to the emergency department [ED]), depending on the urgency of the situation. In previous work by this research team, it has been extremely rare for an ACS patient to report active suicidality that requires intervention.

Similar procedures will be followed if participants report suicidality during the focus group or endorse this PHQ-9 item when completing the survey measures before the focus group begins. These participants will be approached individually after the focus group by the PI or research assistant and further assessed for risk using same protocol described above. As above, if any participants are found to be at imminent risk, the licensed psychologist will be immediately paged to conduct further safety assessments and assist with the obtainment of further evaluation and care as needed, including facilitating a referral to the ED if needed.

Given that all participants will have elevated depression symptoms as part of the eligibility criteria, all participants will be provided with an outline of resources for mental health care and guidelines for how to access this care.

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 involved in the study are minimal. Participants will be informed of potential risks prior to the study, and these risks will be clearly delineated on the study information sheet. Confidentiality will be detailed on the information sheet and discussed in detail so that participants are fully informed of their right to request information and to withdraw from the study at any time without impacting their care. The importance of maintaining confidentiality will be discussed at the beginning of each focus group and intervention group cohort so as to keep information shared within the group as much as possible. Participants will also be made aware of the limits of confidentiality, including that confidentiality would be broken if participants reported thoughts of harming themselves or others, in order to obtain appropriate care for the participant. Participants may choose not to participate in the study or any of the study

procedures without penalty. Those who do agree to participate may withdraw their participation at any time without penalty.

Patients may experience discomfort from discussing psychological experiences and could experience the evaluation as intrusive. Participants who do not find the study to provide a benefit to them may find this upsetting as well. Activities to obtain data through the follow-up assessments may be inconvenient for subjects. All measures will be taken to ensure patient comfort and patients will be informed that they can discontinue their participation in the focus group at any time, and choose not to answer any surveys or survey items that make them uncomfortable. The PI or other psychologist/psychiatrist study staff will be available to intervene if needed (due to patient discomfort or to answer specific questions about the study) during the focus groups.

All data will be encoded only with the study participant number that is linked to personal identifying information only in the study database.

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.

Participants may not benefit from participation in this study. Patients who complete focus groups may obtain benefit from sharing their experiences, and connecting with others with a shared medical problem and finding support and normalizing through hearing others' experiences. Contact with study staff may also provide support and social connection for participants.

Patients will be given the opportunity to hear about the idea of mindfulness training and how it could be used to help ACS patients. Description of mindfulness may enlighten them as to potential means of improving their own emotional states. All patients will also be provided information about resources for mental health care to reduce depression symptoms.

Developing targeted, efficacious, and accessible interventions to treat depression in ACS patients may have important public health benefits. Depression is common and deadly among acute coronary syndrome patients: up to 45% experience elevated depression symptoms, and depression doubles the risk of mortality through behavioral and biological pathways. Mind-body interventions that are accessible and address the underlying pathophysiology of comorbid depression and cardiovascular disease are needed, and MBCT delivered via e-health technologies could address this need. This study will establish preferences, barriers, and facilitators to a remote-delivered MBCT intervention for ACS patients with elevated depression symptoms, in order to develop an intervention that is likely to be feasible and acceptable for testing in a future clinical trial. Thus participation in this study may ultimately result in substantial benefit to future ACS patients.

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.

Approximately 70 individuals between the ages of 35-85 who have had an ACS in their lifetime and have currently elevated symptoms of depression (PHQ-9≥10) will be recruited. The rationale for these criteria is that elevated depression symptoms are significantly, independently predictive of cardiac morbidity and mortality in ACS patients, with more severe depression symptoms conferring greater cardiac risk. Inclusion is not limited to patients with a depression history because those with first episodes after ACS may have the greatest mortality risk. The PHQ-9 (≥10) will be used because it is validated in cardiac patients, reflects clinically significant symptoms, correlates with cardiac events, and has been used successfully in prior NIH-funded studies by this research team.

Women and members of all minority groups will be eligible to participate in this study. The gender and minority composition in this project is expected to largely match the composition of Massachusetts General Hospital's (MGH's) clinical population. Based on outpatient Medicine encounters at MGH in 2015, the demographic distribution of patients is: 49% women; 70% white (non-Hispanic); 12% Hispanic; 10% Black/African American, 6% Asian; 14% other, Native Hawaiian/Pacific Islander, or American Indian/Alaska Native. I expect the clinical population of ACS survivors eligible for this study to be similar to these gender and ethnic distributions.

Patients with active suicidality or past-year psychiatric hospitalization will be excluded to ensure participant safety. Participants with cognitive impairments preventing informed consent will be excluded to ensure all participants have properly consented to be in the study. Non-English-speaking patients will not be included because the research materials and staff are not available to deliver the trial in a language other than English. Children will not be included in this study because ACS is highly uncommon in children. There is a lack of data on data on ACS in children but we can glean from the data on young adults that it is almost completely improbable, as only 3 out of 1000 adults in the US between the ages of 20-39 have experienced an ACS.

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.

For this exploratory focus group, non-English speaking patients will be excluded because there are not study staff who are fluent in Spanish or other non-English languages available to assist with this research, and the budget for this study is not sufficient to cover interpreter services. However, if the overall work in this area does appear to be promising in English with native English speakers, future studies will absolutely be planned to include subjects who speak other languages, since the goal of this research is to develop a program that is applicable and helpful to the broadest set of cultures/languages/people.

For guidance, refer to the following Partners policy:
Obtaining and Documenting Informed Consent of Subjects who do not Speak English
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.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.

Patients will be recruited who have and have not agreed to participate in RODY (Research Options Direct to You). Two different recruitment methods will be used to recruit "RODY yes" and "RODY no" patients.

"RODY No" patients identified from the RPDR will be sent an opt-out letter from their cardiologist and an accompanying letter from the study team. These letters (attached) will describe the study procedures and ask patients to contact the study team within 2 weeks if they would not like to be contacted to hear more about the study. Those who do not opt-out will be contacted via phone by the PI or a trained and CITI-certified research staff member. Patients will be read a brief phone script (attached) informing them of the purpose of the call and asking if they would like to hear more about the research study. Those who agree will be read an information sheet detailing the study procedures, risks and benefits, and confidentiality, and inviting them to participate in the study.

"RODY Yes" patients will receive one opt-out letter from the study team. This letter (attached) will describe the study procedures and ask patients to contact the study team within 2 weeks if they would not like to be contacted further about the study. Those who do not opt-out will be contacted via phone by the PI or a trained and CITI-certified research staff member. Patients will be read a brief phone screen (attached), which will inform them of the purpose of the call and ask if they would like to hear more about the research study, and which will mention that they are being contacted because they agreed to be approached about clinical research studies. Those who agree will be read an information sheet (attached) detailing the study procedures and inviting them to participate. "RODY Yes" and "RODY No" patients will be read the same information sheet, though the opt out letter and phone script will differ.

Only the Principal Investigator and trained research staff will identify and contact patients. Up to approximately 10 calls will be made to a given patient, leaving up to approximately 3 voicemails, before assuming the patient is not interested and no longer attempt to contact them.

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 receive a $30 gift card for participation in the study at the end of the focus group. Participants will also receive a $20 check to provide reimbursement for the cost of travel and parking at the hospital, based on their provided receipts.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf

Remuneration for Research Subjects

https://partnershealthcare-public.sharepoint.com/ClinicalResearch/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.

After identifying potential participants from the RPDR, the study team will mail patients the opt-out letters (one from the cardiologist and one from the study team for "RODY no" patients; one from the study team for "RODY yes" patients). For those who do not opt-out within two weeks, the principal investigator or a trained research staff will contact patients to read the study information sheet over the phone. The researcher will first briefly introduce themselves and the purpose of the phone call and, for patients who are interested in hearing more, the RA will begin the phone screening procedures (see attached phone screen document). For patients who meet eligibility criteria and are willing to hear more about the study, the researcher will review the information sheet (see attached). The information sheet will include a description of all study procedures and information about potential risks and benefits of participation. It will state that participation is voluntary, that participants can refuse to answer questions that make them uncomfortable, that participants can discontinue participation at any time, and that not completing the study will not compromise their medical care. Participants will be given the opportunity to ask questions about their participation throughout the course of their participation in the study. After reviewing the information sheet, the researcher will ask if patients have any remaining questions and then ask if they are interested in participating in the study. The RA will offer to mail a paper copy of the information sheet to the participant if they would like one.

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://partnershealthcare-public.sharepoint.com/ClinicalResearch/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.

For this exploratory study, there will not be interim analyses of samples. However, if it appears that patients do not find the planned research procedures to be acceptable, these procedures will be modified to align with patients' expressed preferences.

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

All PHRC guidelines will be followed with respect to reporting unanticipated problems, including adverse events. Specifically, when a serious or non serious adverse event occurs, the PI will review the event to determine if it was possibly or definitely related to participation in the research. For all unanticipated problems and adverse events deemed related or possibly related to the research, a member of the research team will complete and submit an Other Event report through Insight/eIRB as soon as possible and within 5 working days / 7 calendar days (as defined in the March 2014 Reporting Unanticipated Problems Including Adverse Events report). At Continuing Review, a summary of all unanticipated problems will be provided as per PHRC protocol. Finally, if there are unanticipated problems, especially if serious or recurrent, the PI will amend the protocol if it is deemed necessary to protect the safety and welfare of the participants.

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.

On a weekly basis, the research team will meet to review study progress. At that time, the principal investigator will review information sheet documents, study forms, and procedures completed that week.

The study team will also discuss any procedural difficulties, recruitment issues, and adverse events at this meeting (and before if needed). Investigators will also review information sheet documents and address acute issues in real time throughout the week.

Several measures will be taken to ensure the integrity of data collection/entry/analysis and the fidelity of our intervention. Transcriptions of focus group interviews will be periodically reviewed by the PI and study staff to ensure their accuracy. Furthermore, all transcribed interviews will be coded independently by two individuals, and all disagreements will be adjudicated by the PI.

For guidance, refer to the following Partners policies:

Data and Safety Monitoring Plans and Quality Assurance
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP_in_Human_Subjects_Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://partnershealthcare-public.sharepoint.com/ClinicalResearch/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.

As noted, these risks will be minimized by using participant ID numbers rather than identifying personal data on study documents or audio recordings, and by using locked cabinets/offices and password-protected databases to store personal information. Only study staff (the PI, the research assistant entering data) will have any access to personally identifiable information about participants, and such access will be limited only to information necessary to complete study tasks. Furthermore, the audiotaped recordings of the focus group interviews will be identified only with a number (with this number linked to identifying information that is kept in a password-protected database), will be stored in a password-protected folder on Partners' secure network, and will be destroyed once the time period for keeping research-related data has passed.

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.

N/A

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.

N/A

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.

N/A