Protocol Title: MBCT Delivered Via Group Videoconferencing for ACS Syndrome Patients With Depressive Symptoms

NCT04231097

Protocol version date: 7/7/2020

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

Christina Luberto, PhD

PROTOCOL TITLE

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

FUNDING

NIH/NCCIH 1 K23 AT009715-01A1

VERSION DATE

7.7.2020

SPECIFIC AIMS

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

The proposed research study has the following objectives:

Specific Aim 1: We aim to explore the initial feasibility and acceptability of (a) MBCT adapted for ACS patients; (b) the group videoconferencing delivery medium; and (c) dried blood spot research procedures, to inform refinements for a subsequent pilot RCT.

Hypothesis: The intervention and research procedures will be feasible and acceptable as evidenced by (a) MBCT attendance and retention rates, after-session satisfaction ratings, fidelity ratings, qualitative satisfaction findings, and home practice patterns; (b) number and type of videoconferencing problems, number of participants who require extra training, number of sessions missed due to technical problems, acceptability ratings (e.g. ease, confidence of use), and qualitative satisfaction findings; and (c) blood spot submission rates, number of adequate quality samples, acceptability ratings (e.g., ease, level of pain), and qualitative findings of acceptability.

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), up to 45% have elevated depression symptoms. Even mild elevations in depression symptoms double the risk of mortality after ACS. 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 (≥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.

Our formative qualitative work supports the use of virtual MBCT for ACs patients. We recently conducted a qualitative study (individual patient interviews) to solicit patient's perspectives and needs for a behavioral depression treatment based on MBCT. Patients were open and interested in a mindfulness program, identified a range of symptoms and needs for the intervention to target, offered suggestions for promoting videoconferencing feasibility, and expressed openness to participate in dried blood spot research procedures. The results of this formative work have been integrated into the current proposal.

This proposal is to develop an MBCT intervention adapted for ACS patients and test the feasibility and acceptability of the intervention, delivered via group videoconferencing, for ACS patients with depressive symptoms. This research will incorporate a novel, minimally invasive blood spot data collection procedure to measure inflammation. This innovative project will be one of the first to explore MBCT for ACS patients, and to test MBCT delivered via group videoconferencing. It will generate knowledge about e-health technologies and congruent research methods to apply to other mind-body interventions and patient populations.

Toward these goals, the purpose of the current study is to conduct an open pilot trial to explore the feasibility and acceptability of the adapted MBCT intervention and research procedures, to inform refinements for a future pilot 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."

The current study will employ an open pilot trial to determine the initial feasibility and acceptability of a targeted, virtual MBCT intervention for ACS patients. We plan to enroll approximately N=20 patients (2 cohorts of 10 participants/per cohort, accounting for 20% anticipated lost to follow-up). The MBCT intervention will involve 8 virtually-delivered MBCT sessions (approximately 1.5 hours each), during which participants will be taught how to use evidence-based mindfulness skills to regulate distress and choose healthy behaviors, as well as

learn about cardiac health. We will hold two intervention cohort groups that may be run concurrently or sequentially. Participants involved in the intervention will be asked to complete a brief survey following each session. Within one week before and after the intervention and 3-months post-intervention participants will be asked to complete a series of questionnaires and provide self-collected blood samples. Upon completion of the intervention participants will complete an audio-or video recorded exit interview (approximately 30 minutes). Participant characteristics, inclusion/exclusion criteria and/or intervention design will not differ between the two cohorts.

Inclusion criteria:
1. Lifetime ACS per medical record and/or patient confirmation
2. Current elevated depression symptoms (PHQ-9$\geq$5)
3. Age 35-85 years
4. Access to high-speed internet

Exclusion criteria:
1. Active suicidal ideation or past-year psychiatric hospitalization (per patient report and/or medical record review)
2. Non-English-speaking
3. Cognitive impairments preventing informed consent per medical record review and/or cognitive Screen $\leq$ 4
4. Patient deemed unable to complete the study protocol or has a condition that would likely interfere with the study

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.

Recruitment: Participants will be recruited in several ways. First, patients 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 will have the option to opt-out via phone or email. To address security issues related to email communication, participants will be informed about security in the opt-out letter itself via inclusion of the following text:

> "Please note that emails sent to the study staff from your personal email address may not be secure and could result in the unauthorized use or disclosure of your information. If you want to email the study team despite these risks, Partners HealthCare will not be held responsible. If you do not want to email the study team, you may instead call [XXX RA's phone number]".

For any emails sent by the study team, they will be encrypted using Send Secure, unless patients verbally agree to receive unencrypted email. Patients will receive the following information:

"The Partners HealthCare standard is to send email securely. This requires you to initially set up and activate an account with a password. You can then use the password to access secure emails sent to you from Partners HealthCare. If you prefer, we can send you "unencrypted" email that is not secure and could result in the unauthorized use or disclosure of your information. If you want to receive communications by unencrypted email despite these risks, Partners HealthCare will not be held responsible. Your preference to receive unencrypted email will apply to research studies for emails sent to you from research staff in this study. If you wish to communicate with other research staff at Partners regarding additional studies, your preference will have to be documented with each research group."

Patients who do not opt-out within two weeks will be contacted by phone and screened for eligibility by the study RA, who will be CITI-certified and trained in all research procedures. The RA will explain the study procedures, answer any questions, and complete an eligibility screening, which includes: (a) patient confirmation of ACS history, (b) assessment of current depression symptoms via administration of the PHQ-9, (c) confirmation of patient age, (d) determination of access to high-speed internet, (e) assessment for no active suicidal ideation (per PHQ-9 administration) or past-year psychiatric hospitalization (per patient report), (f) confirmation of English-speaking, (g) confirmation of cognitive capacity via administration of cognitive screener, and (h) determination of patient's ability to complete study protocol and absence of any condition which may likely interfere with participation, per clinician judgment or medical record review (e.g., absence of behavioral or cognitive symptoms that prevent participation in a group setting). The RA will review potentially eligible participants' medical records to confirm possible eligibility (e.g., to confirm ACS history, psychiatric hospitalization history). If participants meet study criteria, they will complete the informed consent process described below. The eligibility screener and phone scripts are included in the IRB submission.

Second, patients will be recruited through advertisements (e.g., flyers, brochures) placed throughout inpatient and/or outpatient hospital clinics. The advertisements will ask patients to contact study staff if they are interested in learning more about the study. The screening procedures will be the same as those described above for RPDR patients, but with an introductory script tailored to the recruitment method. In situations where a briefer ad is more feasible (e.g. virtual postings on iPads and computer screens in clinic waiting rooms), a shortened version of the flyer, detailing the study's purpose and contact information, will be posted. The flyers are included in the IRB submission. Specific phone numbers on the flyers will be filled in based on the contact information for the current RA. These advertisements will also be used to recruit via the MGH Rally program.

Third, patients will be recruited via direct referrals from their providers (e.g., cardiologists, psychiatrists, primary care physicians). We will inform providers about the study (e.g., via short presentations at their team meetings) and provide them with flyers to post in their clinic and/or give to their patients. The patients may either contact study staff directly using the information their provider gave them, and/or the provider will contact the study team with the patient's information so that the study team may reach out to the patient. Providers will obtain verbal permission from the patient for the research team to contact them.

Lastly, patients will be recruited from inpatient cardiac units within MGH. Study staff will review inpatient censuses from MGH cardiac units and automated RPDR-based alerts that identify patients whose available admission information (e.g., laboratory studies) suggests ACS.

Study staff will then review the electronic health record (HER) to assess for clear exclusionary factors (e.g., severe dementia). If none are identified, staff will then approach the clinical team to confirm the cardiac diagnosis and will then ask a member of the clinical team to inquire whether the patient is willing to hear about an optional study. For patients who do not meet criteria or decline to hear about the study, no personally identifiable information will be retained. All patient alerts will be purged from the email/study team system daily. For willing patients, study staff will discuss the study with the patient and assess for additional study criteria using the same screening procedures described above (e.g., PHQ-9 administration). For patients who screen out or decline assessments, we will retain no personal information. Patients who are interested in hearing about the study and completing the screener, but do not want to do so during their hospitalization, will be given the option to be contacted by phone after their discharge. The same screening procedures would be done by phone at that time.

Participant communication: Participants will be asked to specify their preferred contact modalities following informed consent. Study staff will attempt to engage in contact via phone, paper mail, and email to schedule group sessions and send study materials and reminders. Study staff will attempt to engage in contact via email and/or paper mail to send questionnaire batteries, session materials, post-session surveys, and dried blood spot collection kits. At minimum, participants will be asked to provide a home address and telephone number to allow for supplemental contact and delivery of study materials (e.g. intervention guides, gift cards, etc.). Participants will be made aware of Partners policies regarding email per the information below:

Email: Participants will be given the option to communicate (e.g., receive reminders, schedule, etc.) with study staff by email. If the participant chooses email as their preferred method of communication, study staff will explain the encrypted, send secure default feature of emails sent within the Partners Healthcare network. These details are described above in the Recruitment section. In short, patients will be informed that emails sent to the study staff from their personal email address may not be secure and could result in the unauthorized use or disclosure of their information, and if they want to email the study team despite these risks, Partners HealthCare will not be held responsible. Study staff will verify that no sensitive or patient health information will be disclosed in emails and will ensure that the patient understands that by opting-out of the send secure feature, information will not be as secure.

Adapted MBCT intervention. The intervention will be based on Mindfulness-Based Cognitive Therapy (MBCT), an evidence-based, manualized protocol for treating depression symptoms. We will use the existing manualized protocol with adaptations for ACS patients. Following consent, participants will be enrolled in one of two MBCT intervention cohorts. Assignment to each cohort will be based on timing and/or participant scheduling preferences. Participants will be expected to participate in 8-weekly, 1.5-hour virtual sessions, in conjunction with approximately 30 minutes of at-home daily practice. A licensed mental health provider (e.g., LICSW, PhD) trained in the MBCT protocol will deliver the intervention. The interventionist will meet formal training guidelines for MBCT delivery including participation in MBCT workshops, experience leading $\geq$2 MBCT groups with mentorship, and >1 year of experience with group psychotherapy. The interventionist will receive ongoing supervision and feedback from the PI. The MBCT intervention will not be delivered clinically; it is a psycho-educational intervention. We will also send audio recordings used for home mindfulness practice via a send secure Partners email or via Dropbox to participants throughout the intervention.

Intervention delivery. We will deliver the intervention using Zoom, a secure, HIPPA compliant video-conferencing software amenable to study procedures, which we have used successfully in prior studies to deliver mindfulness interventions to other patient populations. Participants will be informed during consent procedures that the videoconferencing system uses a secure, HIPPA-compliant software program. We will explain that although we will do our best to ensure confidentiality on our end and ask group members to not share information outside of the group, we cannot guarantee that other group members will not share the content of the group. Participants will be advised to wear headphones and sit in a quiet place to protect their own and other group members' privacy.

Zoom is routinely used at Partners institutions and there is an enterprise license structure and BAA that is in place and managed by my team. There is no end-user license agreement for individuals to sign. Licenses are assigned by my team and users are sent an email with instructions/links on how to use the system. Only meeting hosts need to install the app. Zoom is a cloud based solution, so participants need only click on the meeting link in the invitation.

Participants will receive training from study staff prior to the start of the intervention regarding the proper use of the video-conferencing software. Study staff will take the necessary steps to ensure that the participant is trained in using the videoconferencing software, and the RA will be available during intervention sessions to assist with any challenges. We will train participants in the videoconferencing program using the training methods ACS patients have asked for in our earlier qualitative work (e.g., instructional handouts, training sessions with an RA).

Intervention fidelity. All sessions will be audio-visually recorded using the capabilities of the videoconferencing system, after reminding the participants that we will do so. The PI will review session recordings and complete a validated MBCT fidelity measure (MBI:TAC; included in the IRB submission); discuss the ratings during supervision with the MBCT interventionist and/or co-investigators; and provide ongoing feedback to the interventionist as needed.

Secure storage of recordings. Audio-video files will be labeled with the intervention group number, participant ID numbers, session number, and date. Contact information and personal identifying information about the participants will be held in separate, password-protected files on a secure Partner's network. All audio-video files will be stored on a password-protected drive on a secure Partners' network immediately following each intervention session and will be destroyed 7 years following the completion of the study.

Data collection. Study assessments include a battery of self-report surveys administered at baseline, post-intervention, and 3-month follow-up; session satisfaction surveys administered after each intervention session; post-intervention individual exit interviews (conducted via telephone or videoconference); blood spot samples self-collected by participants at baseline, post-intervention, and 3-month follow-up (submitted to the research team via paper mail); and home practice logs submitted between each intervention session. Surveys and home practice logs may be completed via REDCap, email, paper mail, phone, or videoconferencing depending on patients' preferences. Data collection will also consist of viewing and extracting data from the EHR of enrolled participants to assess medical and demographic variables (e.g. medical diagnoses, medications, cardiac rehab attendance). See Figure 1 for an overview.

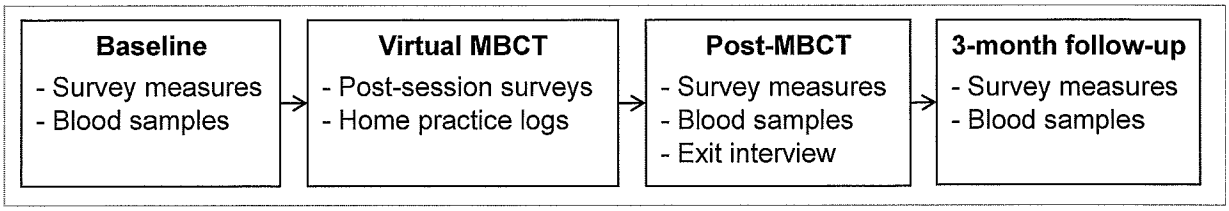

Figure 1. *Overview of open pilot data collection procedures*

Survey measures. The self-report survey measures will be administered within approximately one week before and after the intervention and at 3 months post-intervention. This battery will include the following validated self-report surveys: PHQ-9 (depression symptoms), FFMQ-15 (mindfulness), PANAS-PA (positive affect), RRS (rumination), SOFI (self and other compassion), IRI (empathy), MOS-SAS (adherence), one item from the SF-12 (health-related quality of life), PROMIS-PF (physical function), HADS (anxiety and depression), and CES (resilience). The baseline survey will also include the Expectancy Questionnaire (EQ) to assess expectations about the utility of the intervention. The post-intervention survey will also include a group cohesiveness measures to assess perceived connection with other group members as well as intervention satisfaction questions to assess acceptability. The 3-month follow-up survey will include questions about continued mindfulness practice. The baseline survey, post-intervention survey and post-intervention survey will all include questions related to COVID-19. All three survey batteries are included in the IRB submission.

Post-session surveys. The post-session surveys will be administered immediately after each of the 8-sessions and will assess participants' perceptions, and likes and dislikes, of specific intervention components. Prior to each session participants will be asked to email, mail, or complete via REDCap a record of their at-home mindfulness practice since the previous session. The post-session surveys and home practice log are included in the IRB submission.

Exit interview. Upon completion of the intervention, participants will be asked to complete a 30-60 minute exit interview via phone or video conference. These interviews will be audio- and/or video-recorded for transcription.

Dried blood spots. Within one week before and after the intervention and 3-months-post intervention, participants will be asked to provide self-collected whole dried blood spots to assess IL-6, CRP, and TNF-α using a minimally invasive finger skin prick technique, which involves pricking the finger with a lancet, milking the finger to produce 5-10 drops of blood onto filter paper, allowing the blood spots to dry, and mailing it to the study team at MGH in a secure envelope. Prior to the start of the intervention, an RA will guide the participant in self-collecting blood samples via a videoconference call, phone call, and/or in person (per the participant's preference). Participants will be sent a video link for a guided demonstration of the procedure and/or written instructional handouts. The RA will ask the participant a series of questions to gauge understanding, provide corrective feedback, and answer any questions the participant might have before proceeding to guide the participant in the procedure. Skin prick procedures are safe for patients on beta-blockers and anticoagulants. Participants may also receive written instructional materials.

Participants will be asked to allow the sample to dry overnight, document the date the sample was taken on the filter paper, and mail it to the study team at MGH the next morning. Samples

will be received by the RA, who will mark the date of receipt in the study database. Samples can be in ambient air for up to 2 weeks without degradation. We will ask participants to mail the samples within 24 hours of taking them to minimize the time samples are in ambient air. If samples are received beyond 2 weeks of the date indicated on the filter paper, we will ask participants to provide another sample, and participants will be made aware of this possibility in the consent form. Once received, the RA will bring the samples to be stored in a -20°C freezer in the MGH Clinical Research Center lab or mail them to our collaborator at the Laboratory for Human Biology Research at Northwestern University for storage and processing. Blood spots can be frozen at this temperature for several years without degradation.

When initially mailing the blood spot kit to participants, the RA will indicate the participant's study ID number on the filter paper. Participants will be informed not to write any personally identifying information on the filter paper. This will keep the blood samples de-identified.

Collecting whole blood spots with filter paper has been used in hospitals for decades to collect blood from newborns, and it has proven to be a safe and effective means for collecting and transporting samples in several large NIH-funded field-based studies. The Centers for Disease Control and Prevention have maintained independent quality control efforts and have reported that these approaches can achieve the same level precision and reproducibility of standard blood collection methods. Our collaborators at Northwestern University have pioneered this technique as leaders in the development, validation and application of whole dried blood spots as a convenient means for collecting, transporting, and processing blood samples from community settings and mind-body intervention research including clinical trials.

Measured Outcomes: The primary outcomes are feasibility and acceptability of the intervention and research procedures. Study staff will record all feasibility outcomes throughout recruitment, screening, enrollment, and the intervention, data collection, and follow-up phases.

Feasibility outcomes for recruitment include: ≥70% of patients reached consent to screening, ≥70% meet screening criteria, ≥70% of eligible enroll, and enrolling approximately N=20 participants within 1-2 months. Feasibility for eligibility criteria include: <20% ineligible due to each criterion, reasons for ineligibility, reasons for refusal, and characteristics of refusers. MBCT feasibility will be measured by: ≥75% session attendance, ≥75% post-assessments completed, ≥70% follow-up assessments completed, fidelity checklist score ≥80%, and ≥75% complete home practice at least 3 days/week. Videoconferencing feasibility will be assessed by: < 20% of connections dropped during session; <20% of sessions missed due to technical problems; number (Mean <2.0) and types of problems, <20% ask for extra training and type of extra training needed. Blood spot feasibility will be assessed by ≥75% of samples submitted at baseline and post-intervention, ≥60% submitted at follow-up, and 80% of samples of adequate quality.

Acceptability outcomes will be assessed via post-session surveys, post-intervention surveys, and exit interviews. MBCT acceptability will be assessed by average scores ≥7.5 on ratings of session helpfulness, enjoyment, relevance, and utility of session components (scale of 1 = not at all to 10 = very much). Overall program satisfaction will be assessed by M≥7.5 regarding overall program satisfaction, ≥75% of participants reporting that they plan to use the skills in the future, ≥75% reporting that they would recommend the program to others, and ≥60% reporting continued mindfulness practice on the follow-up survey. Likes and dislikes will be explored in the exit interviews. Videoconferencing acceptability will be assessed in terms of ease and

confidence of use (1 = not at all to 10 = extremely, M $\geq$ 7.5), interference of technical problems (1= none to 10 = extreme, M<2.0), audiovisual quality and overall satisfaction (1= poor to 10 = excellent, M$\geq$7.5), and themes related to pros and cons and suggestions for improvement in the exit interviews. Blood spot acceptability will be assessed by ratings of ease of data collection and submission (1 = not at all, 10 = extremely; M $\geq$ 7.5), level of pain (1 = none, 10 = extreme, M < 2.0), and concerns and suggestions for improvement expressed in the exit interview.

Secondary, exploratory outcomes include symptom outcomes and process variables, corresponding to each of the validated, self-report survey measures described (e.g., depression symptoms, mindfulness).

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.

The standard of care for depression treatment at Partners involves psychotherapy, particularly cognitive behavioral therapy, and/or pharmacotherapy. The study procedures differ from standard of care in that the MBCT intervention is a form of cognitive behavioral therapy with the addition of mindfulness training, and in that the study procedures will not include administration of pharmacotherapy. All patients enrolled in the study will still be able to access psychotherapy and pharmacotherapy (e.g., through the MGH Psychiatry Department). Engagement in other depression treatments is not an exclusion criterion for the current study. Patients will be informed about these alternative treatment options in the consent form.

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 completing the survey questionnaires or exit interview, participating in the intervention mindfulness trainings or discussions, and/or completing the blood spot finger-prick procedures. Participants who do not find the study to provide a benefit to them may find this upsetting as well. All possible measures will be taken to ensure patient comfort and participants will be informed that they could exit the study at any point with no penalty. The PI (licensed clinical psychology) will be available while intervention groups are being conducted to intervene if needed (due to patient discomfort or to answer specific questions about the study). Participants will be informed that they can choose not to complete any surveys or answer any specific survey items or exit interview questions that make them feel uncomfortable, and that they do not need to complete the blood spot procedures. All of these procedures are consistent with sound research design and do not unnecessarily expose subjects to risk.

The process of collecting a dried blood spot sample is relatively painless and non-invasive; however, participants may face minimal discomfort when completing this procedure. Prior to the dried blood spot sample collection, participants will be informed that the procedure may involve mild, temporary pain at the finger prick site and will be provided with suggestions for minimizing any pain that is bothersome (e.g., putting ice on the site). Participants will be sufficiently trained by study staff in how to self-collect their blood samples at home. If needed, participants will be given the option to come to the hospital to take their blood samples with RA

support. Participants will be given the option to opt out of any dried blood spot collection points, for any reason. Participants who oppose the provision of dried blood samples will not be excluded from additional study procedures. In our previous study, it was common for ACS patients to already have experience using the blood spot finger-prick technique for their healthcare and almost all participants expressed comfort and willingness to complete this procedure as part of a research study.

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. The process of submitting blood spot samples via paper mail may pose a risk of samples getting lost in the mail. To minimize this risk, participants will be asked to inform the RA when they mail the sample, and the RA will contact the patient to let them know when the sample has been received. These samples will only be labeled with the participant's study ID number and not with any personally-identifying information.

Participants will be advised to wear headphones and sit in a quiet place during each virtual intervention session. We will instruct participants to maintain the confidentiality of group members by not discussing any events or information associated with other group members outside of the group. Added attention will be taken during the informed consent process to explain this risk to participants.

The audiotaped or video-taped recordings of the individual exit interviews and MBCT intervention sessions will be identified only with the participant's study ID number or intervention group/session number (with this number linked to identifying information that is kept in a password-protected database). These recordings will be stored in a password-protected folder on Partners' secure network, and will be destroyed 7 years following the completion of the study.

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.

As the intervention is psycho-educational in nature, and participants do not need to physically come to the hospital to participate in any study procedures, there is no risk of physical injury to participants. There is a risk of mild, temporary physical discomfort due the blood spot procedures, which will be handled as described above. The blood spot finger-prick technique is safe for ACS patients. Participation is voluntary for all subjects. As explicitly stated in the informed consent documents, participants may withdraw from participation at any time by notifying study staff. Participants will not be required to provide a reason for withdrawal. Participants will be reminded that they can withdraw from the study at any point during their participation.

The main psychosocial safety concern related to patients in this study is worsening depression symptoms and/or suicidal ideation. Subject safety regarding mood and 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 or following the intervention. Moreover, our eligibility criteria require only minimal depression symptoms and thus we do not expect to have a severely depressed sample.

During the eligibility screening procedures, participants will be administered the Patient Health Questionnaire-9 (PH-9) over the phone. If any patient 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 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 risks through a series of structured questions, with specific instructions at each step based on the patients' response. It begins 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 risks (e.g., plan, intent, past suicide attempts) and immediately notify the PI (a licensed clinical psychologist) to conduct further assessment. The RA will attempt to keep the patient on the phone until the PI has reached them. The PI will conduct detailed suicide assessment of patients with active suicidality and 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 our previous work, it has been extremely rare for an ACS patient to report active suicidality that requires intervention.

Upon enrollment, the RA will also conduct proactive safety planning with all participants in the following ways: (1) asking participants to identify 1-2 safety contacts that we would contact in the event that participants become at risk, (2) working with participants to identify the emergency department nearest to their home; (3) and instructing patients to go to this emergency room if they feel unsafe, and inform research staff once they are in a safe place (e.g., hospitalized or back at home). Participants will be asked to report any worsening symptoms to the interventionist during sessions, or in between sessions by contacting the study RA.

For enrolled participants, the PHQ-9 will be administered at baseline, post-intervention, and 3-month follow-up, which will allow us to monitor for worsening depression symptoms. The RA will review changes in participant's PHQ-9 scores over time and contact the participant to discuss any concerns, asking about their symptoms, needs, and concerns about staying in the study, and conducting an initial safety assessment as needed (as described above). The same procedures as described above will be followed if participants endorse suicidality on PHQ-9 item 9 when completing the measure as part of any of the surveys. REDCap will be set up to send automatic alerts to the study staff for any PHQ-9 item 9 responses greater than zero. Participants will be contacted within 24 hours.

The interventionists will observationally monitor participant's symptoms during each weekly intervention session. If the interventionists become concerned based on a participant's presentation during a session (e.g., per their clinical observation or expressed SI by a

participant), they will call the participant by phone individually immediately after the session to check in about the participant's symptoms and conduct a safety assessment if needed (following the protocol outlined above). The interventionist will be a licensed mental health provider trained in conducting safety assessments. Interventionists will instruct patients at the start of the first session, and periodically remind them throughout the intervention, that if they experience suicidal thoughts or worsening depression symptoms at any point during the study, they should let the interventionist, study staff, and/or their doctors know.

The objective criteria for removal from the study is worsening psychiatric symptoms that become psychiatrically unstable that precludes their participation (e.g., constitute danger to self or others). The RA and interventionist will inform the PI of any concerns about a participant's symptoms and about any contact with participants regarding these concerns. They will let the participants know that if it seems unsafe for them to remain in the study, the PI will contact them. In cases where depression symptoms are worsening but do not constitute necessary removal from the study, the PI will discuss the concerns with the participant, give them the option to exit the study if they would like, and assist them in connecting to a higher level of care if needed (e.g., by providing mental health referrals).

Participants will be provided with an outline of resources for accessing mental health care at the completion of the study.

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.

As in any research study, there is a small risk that confidentiality may be breached; all efforts to minimize this risk will be taken, as outlined above. Patients may face discomfort with intervention procedures, survey questionnaires, exit interview topics, and providing dried blood spot samples. All measures to maintain participant safety, satisfaction and comfort are detailed above.

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 this study. Participants in the current study may observe a reduction in mood symptoms. It is hoped that the intervention will result in improved scores on depression symptom measures. The current study may provide training in coping skills for managing depression and improving health behaviors. It may also provide emotional benefits for participants to share and receive support with their peers.

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 ACS patients with up to 45% experiencing at least mild depression symptoms. Even mild depression symptoms double the risk of death in ACS patients. Mind-body interventions that are accessible and address the underlying pathophysiology of comorbid depression and cardiovascular disease are needed, and the MBCT intervention being tested in the current stay has the potential to address this need. This study will establish the feasibility and acceptability of the intervention and inform targets for refinement in a future pilot RCT. Thus, participation in this study may result in the development of an innovative, efficacious, and accessible depression treatment that can have 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 20 individuals between the ages of 35-85 who have had an ACS in their lifetime and have currently elevated symptoms of depression (PHQ-9$\geq$5). The rationale for these criteria is that elevated depression symptoms are significantly, independently predictive of cardiac morbidity and mortality in ACS patients. Inclusion is not limited to patients with a depression history because those with first episodes after an ACS may have the greatest mortality risk. It is not limited to those with moderate-severe depression symptoms as those with mild depression symptoms are also at an increased risk, perhaps at even greater risk than those with moderate-severe symptoms. The PHQ-9 ($\geq$5) 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. We 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.

Only participants who can read and speak English will be included in the current study as the intervention will be delivered in English due to the capabilities of the research team, and because not all assessment measures have been validated for use in non-English speaking populations. 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://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.

Study staff will engage in multiple recruitment modalities to obtain a diverse sample of study participants. First, patients will be recruited through the RPDR. We will include patients 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. Patients will have the option to opt-out via email. To address security issues related to email communication, participants will be informed about security in the opt-out letter itself and the following text will be included, "Please note that emails sent to the study staff from your personal email address may not be secure and could result in the unauthorized use or disclosure of your information. If you want to email the study team despite these risks, Partners HealthCare will not be held responsible. If you do not want to email the study team, you may instead call 617-726-9131". For any emails sent by the study team, they will be encrypted unless patients verbally agree to receive unencrypted emails. Patients will receive the following information: "The Partners HealthCare standard is to send email securely. This requires you to initially set up and activate an account with a password. You can then use the password to access secure emails sent to you from Partners HealthCare. If you prefer, we can send you "unencrypted" email that is not secure and could result in the unauthorized use or disclosure of your information. If you want to receive communications by unencrypted email despite these risks, Partners HealthCare will not be held responsible. Your preference to receive unencrypted email will apply to research studies for emails sent to you from research staff in this study. If you wish to communicate with other research staff at Partners regarding additional studies, your preference will have to be documented with each research

group." 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 undergo informed consent, described below.

"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 undergo eligibility screening (attached). Those who are eligible and interested will undergo informed consent, described below. "RODY Yes" and "RODY No" recruitment procedures will be the same, though patients will receive different letters though the content of the opt out letter and phone script will differ accordingly.

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 attempting to contact them.

Second, patients will be recruited through flyers placed throughout inpatient and/or outpatient hospital clinics. The advertisements will ask patients to contact study staff if they are interested in learning more about the study, and the screening procedures will be similar to those described above for RPDR patients. In situations where a briefer ad is more feasible (e.g. virtual postings on iPads and computer screens in clinic waiting rooms), a shortened version of the flyer, detailing the study's purpose and contact information, will be posted. The flyers are included in the IRB submission. Specific phone numbers on the flyers will be filled in based on the contact information for the current RA. These advertisements will also be used to recruit via the MGH Rally program.

Third, patients will be recruited via direct referrals from their providers (e.g., cardiologists, psychiatrists). We will inform providers about the study (e.g., via short presentations at their team meetings) and provide them with advertisement materials to give to their patients. The patients may either contact study staff directly using the information their provider gave them, and/or the provider will contact the study team with the patient's information so that the study team may reach out to the patient. Providers will obtain verbal permission from the patient for the research team to contact them.

Lastly, patients will be recruited from inpatient cardiac units within MGH. Study staff will review inpatient censuses from MGH cardiac units and automated RPDR-based alerts that identify patients whose available admission information (e.g., laboratory studies) suggests ACS. Study staff will then review the EHR to assess for clear exclusionary factors (e.g., severe dementia). If none are identified, staff will then approach the clinical team to confirm the cardiac diagnosis and will then ask a member of the clinical team to inquire whether the patient is willing to hear about an optional study. For patients who do not meet criteria or decline to hear about the study, no personally identifiable information will be retained. All patient alerts will be

purged from the email/study team system daily. For willing patients, study staff will discuss the study with the patient and assess for additional study criteria using the same screening procedures described above (e.g., PHQ-9 administration). For patients who screen out or decline assessments, we will retain no personal information. Patients who are interested in hearing about the study and completing the screener, but do not want to do so during their hospitalization, will be given the option to be contacted by phone after their discharge. The same screening procedures would be done by phone at that time.

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 reimbursed using the Partners Forte Payment system. Forte Payments is a cloud-based application that provides subjects with a reloadable Visa card that is credited with fixed stipends following specified data collection points. Participants will be informed of Forte policy via the informed consent form. After agreeing to participate in the study, participants will also be asked to sign a "Forte Participant Payment Card Acknowledgement of Receipt" form, to certify their understanding of Forte Payment polices. The form will require the subject to print and sign their name and provide their social security number. When mailing "Forte Participant Payment Card Acknowledgement of Receipt" forms is not an option (e.g. due to COVID work restrictions), participants will be asked to complete the form electronically via REDCap. Similar to the electronic consent process detailed below, study staff will email participants a link to an electronic version of the form. Participants will be given time to review Forte guidelines, and when ready will review and electronically sign the "Forte Participant Payment Card Acknowledgement of Receipt" form with study staff over the phone. Participants will then be provided with the option of receiving a mailed copy of the completed form through send secure email or through paper mail. All paper versions of the Forte acknowledgement forms will be stored in a locked, study cabinet.

Participants will be remunerated up to $145 via a reloadable debit card. Participants will receive $10 for each survey battery completed within one week before and after the intervention and 3-months post-intervention (e.g. up to $30 total). Participants will receive $5 for each of the 8-post session survey completed (e.g. up to $40 total). Participants will receive $15 for the completion of an individual exit interview. Participants will receive $20 for each of the three dried blood spot sample collections (e.g. up to $60 total). Participants will be remunerated via their reloadable debit card directly following their completion of the aforementioned study procedures. Participants will participate in the intervention free of cost.

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.

A member of the study staff will determine patients' eligibility status, explain the purpose of the study and study procedures, and answer any questions prior to completing informed consent per the information below. Patients will be provided with the informed consent document electronically, via paper mail, or in person. The informed consent document will then be carefully reviewed with study staff via discussion with the patient either in person or by phone or videoconference. After the form is reviewed and all of the patient's questions have been answered, the patient may then sign and submit the form electronically, via paper mail, or in person (for inpatient recruitment). All patients will be provided with study staff contact information if any questions or concerns regarding the research arise.

As stated above, member of the study staff will obtain informed consent in one of three ways, depending on patient preference: 1) electronically (via REDCap or emailed pdf of the consent form), 2) via paper mail correspondence, or 3) in person (for patients who are recruited while inpatient). Participants who opt to receive the consent materials via paper mail will be asked to provide a mailing address. Participants who opt for electronic consent will be made aware of security concerns related to email communication (as described earlier) and, after specifying their preference for encrypted or unencrypted email, be emailed the informed consent portal via REDCap or electronic copy of the consent form.

Electronic Informed Consent Process (EIC):
Participants will be emailed the informed consent portal via REDCap. The REDCap link will connect the participant to an encrypted REDCap portal; the Electronic/Paperless Consent Template Project will be used. Once the participant confirms receipt of the EIC form link, they will be prompted to enter in their full name and birthday to access the informed consent form and verify their identify. This portal will have the electronic (paperless) consent form, exactly identical in content to the paper version, to guide the participant, through the consent discussion with study staff over the phone. The participant will be given ample opportunity to ask questions and take their time to consider their participation. If a participant would prefer, they may return to the EIC portal as many times as they would like to review the consent form on their own time. When ready to sign consent, participants will digitally sign and date/time the consent form. Additionally, the participant will be prompted after signing to indicate the method through which they would like to receive a copy of the consent form for their record: digitally or through hard copy. If a participant would like to receive a copy of the consent form digitally, they will be asked of their preference to receive the email as encrypted, the default, or opt-out and receive the

email unencrypted. These options allow participants to be informed of what an encrypted (Send Secure) email would appear as in their inbox and the steps to get into the email, or alternatively, to give permission receive the email without this extra layer of security but in a more accessible format. Partner's Healthcare language concerning the Send Secure feature is included to assist in this decision. Study staff will confirm receipt of the digital signature and will sign and date the consent form as the consenting study staff member. At any point, if a participant would prefer to receive a hard copy of the consent form, the EIC process will stop, and study staff will commence the phone and mail correspondence process for informed consent.

Participants may also elect to receive an electronic copy (pdf) of the consent form via email, according to the email security procedures previously described. In this case the participant could print and sign the form and either scan/email or send via paper mail back to the research team.

Paper mail correspondence:
If the participant would prefer to complete the informed consent process via paper mail, study staff will start by facilitating the informed consent discussion over the phone. Once all questions are answered to the satisfaction of the participant, study staff will mail 2 signed copies of the informed consent form for the participant to review, sign and mail back one copy at their convenience. Participants will be provided with a pre-stamped, pre-addressed envelope for their return. Study staff will maintain one copy of the informed consent form for study records, participants will be instructed to maintain one copy for personal reference.

In-person Informed Consent Process
Study staff will go through the informed consent discussion in a hospital or private room to protect patient confidentiality and answer any questions. Upon consent, study staff will maintain one copy of the informed consent form for study records, and participants will be instructed to maintain one copy for personal reference. Patients who would like more time to consider participation are able to take the forms home with them to review, and if interested, they may complete the consent process electronically or proceed to mail back the consent forms.

Following consent, the participant will be asked to provide and clarify their preferred contact modalities for their participant throughout the study. They will be informed that they can change these preferences at any time. Study staff will document the outcome of this conversation and proceed with participant contact accordingly.

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.

The principal investigator is ultimately responsible for data and safety monitoring. If study staff become aware of any adverse events, the event will be reported immediately to the PI. All data will be entered into a password protected database and cleaned for accuracy. Electronic participant tracking databases will be stored on a secure server. Data collected using REDcap will identify patients only by study ID. The main safety risks for the study include the potential for psychological discomfort with surveys.

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 consent form documents, study forms, and/or research 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 address acute issues in real time throughout the week as needed.

Regarding survey data, a member of study staff will verify that all items on all questionnaires have been addressed. Data will be checked for out of range values using frequency distributions prior to analyzing the data. For blood spot samples, our collaborators at Northwestern University will inform us of the number of samples that were not of adequate quality for analysis and the participant ID numbers of these samples. The Principal Investigator will be responsible for ensuring compliance with IRB procedures.

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.

In terms of risks to privacy, there is an inherent risk in the discussion-based group intervention format. There is a risk of a participant sharing personal information gathered from the groups

with his or her family, friends, co-workers, doctor, etc. To minimize this risk, participants will be asked not to share any personal information shared within the group sessions with outside sources. During the consent process, participants will be asked to consent to the rules of confidentiality and will be informed that the research team cannot 100% guarantee that all participants will maintain confidentiality. Participants will also be made aware that confidentiality would be broken if an individual seems at risk of harming themselves or others, in order to obtain appropriate care for the person. Study staff will monitor the intervention groups to determine whether any information raises questions about safety risk.

The PI will oversee all data collection and analysis and will ensure the integrity of the project. As noted above, study data will not be linked to any identifying information; rather study ID numbers will be assigned and used to identify participants. All study forms and data will be stored in an access-restricted database, in which only trained study staff will have access to.

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.

De-identified dried blood spot samples will be sent to our collaborator Dr. David Victorson at Northwestern University for storage and/or processing. All samples will be labeled with the patient ID, date of collection, time of collection, and time point (baseline, post-intervention, 3-month follow-up). We will place a freeze pack inside of an insulated shipping container and will place sealed plastic bags containing the samples into a box. We will seal the box tightly with tape and ship specimens via courier to Dr. Victorson's Consciousness in Health Lab at the Northwestern University Feinberg School of Medicine.

Dr. Victorson will securely store the samples in his locked lab at Northwestern before bringing them for processing to his collaborator Dr. Thomas Dade at the Laboratory for Human Biology Research at Northwestern University. The blood samples will not contain identifiers that could be used by the outside collaborators to link the data to individual subjects; they will be labeled with participants' study ID numbers and not any personally-identifying information, and only Partner's study staff will have access to the data file linking participant's personal information to their study ID number.

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.

Blood samples will not be stored for future use not described in the protocol. Once blood samples are processed for the purposes described in this protocol, they will be destroyed.

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.

We will not receive blood samples from collaborators outside of Partners.