Remote-delivered Mindfulness-Based Cognitive Therapy to Target Fear of Recurrence among SCAD Survivors

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MASS GENERAL BRIGHAM HUMAN RESEARCH OFFICE
PROTOCOL SUMMARY

Answer all questions accurately and completely in order to provide the Mass General Brigham IRB Office 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

Remote-delivered Mindfulness-Based Cognitive Therapy to Target Fear of Recurrence among SCAD Survivors

FUNDING

NIH

VERSION DATE

3/09/22

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: To explore feasibility and acceptability of UpBeat-MBCT for SCAD survivors and make treatment refinements (2 sequential groups of approx. N=8 survivors/group). Hypotheses: (1) The intervention will be feasible (enrollment, retention, attendance ≥70%); and (2) acceptable (satisfaction ratings ≥70%, exit interview themes of satisfaction).

Specific Aim 2: To explore feasibility of the research procedures (pre-post intervention surveys, daily diaries, actigraphy use). Hypothesis: Each research procedure will be feasible (≥70% completion).

Specific Aim 3 (exploratory): To explore changes in psychological and behavioral variables and their associations. **3a:** To explore changes in psychological variables. Hypothesis: Participants will report improvements in each UpBeat-MBCT mechanism (non-judgmental body awareness, attention regulation, cognitive de-centering, distress tolerance), FOR process (interoceptive bias, intolerance of uncertainty), and FOR outcome (FOR severity, cardiac anxiety). **3b:** To explore changes in behavioral variables. Hypothesis: Participants will report improvements in sleep and physical activity outcomes. **3c:** To explore associations between changes in psychological and behavioral variables. Hypothesis: Changes in psychological variables will be correlated with changes in behavioral variables.

BACKGROUND AND SIGNIFICANCE

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

Spontaneous coronary artery dissection (SCAD) is an important yet understudied cause of acute cardiac events, involving the sudden separation of layers of a coronary artery wall, leading to obstructed blood flow. SCAD primarily affects healthy women with no cardiovascular risk factors, accounting for up to 40% of cardiac events in young women.

The 10-year recurrence rate is 30%, but SCAD recurrence cannot be predicted. Given the unpredictable onset and disease course, SCAD survivors commonly struggle with high fear of recurrence (FOR). Critically, elevated FOR is associated with poor health behaviors including poor sleep and physical inactivity, which further increase the risk of future cardiac events. A scientific statement from the American Heart Association identified a need for interventions to improve outcomes after SCAD, but there have been no interventions developed to improve FOR or health behaviors in SCAD survivors.

Mindfulness-Based Cognitive Therapy (MBCT) has the potential to improve FOR and health behaviors in SCAD survivors. Evidence supports the efficacy of MBCT to improve FOR, sleep outcomes, and physical activity, in other patient populations. MBCT is an 8-session group intervention that combines cognitive behavioral therapy with mindfulness meditation to teach non-judgmental awareness and self-regulation of attention toward the present moment. Our published empirical model explicates how MBCT can reduce FOR via increases in four mechanisms of action (non-judgmental body awareness, attention regulation, cognitive de-centering, distress tolerance) that directly target reductions in two key FOR processes (interoceptive bias, intolerance of uncertainty), resulting in improvements in FOR severity and, subsequently, health behaviors.

Through the PI's current NIH K23 award, our team has already adapted MBCT to target the needs of acute cardiac event survivors. The adapted intervention (UpBeat-MBCT), was developed through qualitative interviews with 22 cardiac event survivors, primarily men who survived acute coronary syndrome (Insight Protocol # 2018P001000). Results revealed a multitude of quality of life concerns including FOR, sleep problems, and physical inactivity. We adapted MBCT to target these concerns and be appropriate for group videoconferencing delivery (Insight Protocol #2020P000045). Given the patient-informed adaptations and MBCT mechanisms of action, UpBeat-MBCT is hypothesized to be feasible, acceptable, and improve FOR and, thereby, health behaviors, for SCAD survivors. Given the unique sociodemographic and medical characteristics of SCAD survivors, there may be ways to further target UpBeat-MBCT to optimize relevance and benefits for this unique population.

This study proposes to adapt the UpBeat-MBCT intervention for SCAD survivors and test the feasibility and acceptability of the intervention, delivered via group videoconferencing in an open pilot trial. We will explore changes in psychological and behavioral variables. This innovative project will the first to explore MBCT for SCAD survivors. It will generate knowledge about e-health technologies and congruent research methods to apply to other mind-body interventions and patient populations.

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 Mass General Brigham 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 Mass General Brigham 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 UpBeat-MBCT intervention for SCAD survivors. We plan to enroll approximately N=20 participants (approx. n=8 survivors/group, accounting for 20% anticipated lost to follow-up). The UpBeat-MBCT intervention will involve 8 MBCT sessions (approximately 1.5 hours each) delivered via synchronous group videoconference, which combines cognitive-behavioral therapy, mindfulness meditation, and cardiac health behavior promotion. During each session, participants will be taught how to use evidence-based mindfulness skills to reduce fear of recurrence and promote positive health behaviors (and physical activity). We will hold two intervention cohort groups that will be run sequentially. Participants in the intervention will be asked to complete a full survey battery of the measures before and after the intervention, and wear an actigraphy device (e.g., to measure physical activity and sleep patterns) for 7 consecutive days within the 1-2 weeks before and after the intervention. In addition, participants will be asked to complete a daily diary of abbreviated measures for 1-2 weeks before and after the intervention. Upon completion of the intervention, participants will complete an audio- or video-recorded exit interview (approx. 45-60 minutes).

Inclusion criteria:

1. Age ≥ 18
2. Cardiologist-confirmed diagnosis of SCAD in the past 3-18 months
3. Internet access (via computer or mobile device)
4. English-speaking and reading

Exclusion criteria:

1. Terminal illness with life expectancy <1 year
2. Severe mental illness requiring urgent psychiatric intervention or past-year psychiatric hospitalization
3. Significant cognitive impairment preventing informed consent
4. Deemed unable to complete research procedures
5. Unavailable for intervention sessions (e.g., schedule conflicts)

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 Mass General Brigham will not participate in the pharmacokinetic portion of the study." Describe study endpoints.

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/or email to schedule group sessions, send study materials and reminders, and send questionnaire batteries and daily diary surveys. At minimum, participants will be asked to provide a home address, telephone number, and email address to allow for contact and delivery of study materials (e.g., intervention materials, actigraphy device, gift cards, etc.). Participants will be made aware of MGB 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 MGB Healthcare network. Patients will receive the following information:

> "The MGB 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 MGB. 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, MGB 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 MGB regarding additional studies, your preference will have to be documented with each research group."

Adapted MBCT intervention:
UpBeat-MBCT represents our recent adaptation of the evidence-based MBCT protocol, targeted to the needs of acute cardiac event survivors based on the study PI's K23 qualitative research (IRB Protocol Number 2018P001000) and open pilot trial in patients after acute coronary syndrome (IRB Protocol Number 2021P000544). It is a virtual 8-week group intervention (approx. 90-minute weekly sessions) that combines cognitive-behavioral therapy, mindfulness meditation, and cardiac health behavior promotion. There is 15-20 minutes of daily mindfulness practice between sessions. Participants are provided an optional home practice record form that they can use to keep track of their practice between sessions if they would like. The UpBeat-MBCT will be tested in the first intervention group, then refined to further target the intervention to SCAD survivors, creating SCAD-MBCT for testing in the second group.

Intervention delivery:
We will deliver the intervention using Zoom or a HIPPA compliant video-conferencing platform approved by MGB for use in research virtual visits. Zoom is 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 (IRB Protocol Number 2020P000045). 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 MGB 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 and which we have used successfully in our prior studies (e.g., instructional handouts, training sessions with an RA; IRB Protocol Number 2020P000045).

Intervention fidelity. The intervention will be delivered by the PI, who is a licensed clinical psychologist highly trained in the MBCT protocol, and who developed the adapted UpBeat-MBCT protocol in prior studies. All sessions will be audio-visually recorded using the capabilities of the videoconferencing system, after describing this during informed consent and reminding the participants that we will do so at the start of the first session. The PI and/or another trained study staff clinician will review session recordings and complete a validated MBCT fidelity checklist measure (MBCT-AS; included in the IRB submission). We will use the session

recordings and fidelity assessment to ensure that the intervention is being delivered as intended and are in adherence to the MBCT protocol. Video recording of MBCT sessions is necessary for ensuring that the intervention is delivered properly. Intervention fidelity is a critical aspect of behavioral intervention research, and video recording of intervention sessions allows for assessment of interventionist body language, non-verbal communication, and connection with participants, which cannot be obtained from audio alone, and are critical to the delivery of the MBCT intervention in particular. We are using video recording of MBCT sessions in our other NIH-funded trials of MBCT (IRB# 2020P000045; 2021P000544). Regarding the exit interview, we revised the protocol summary to state that we will only store audio recordings. We will conduct the interviews via Zoom but will ask participants to turn their camera off and/or only save the audio file of the Zoom recording.

Secure storage of recordings. Audio-video files will be labeled with the intervention group number, 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 MGB 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 pre-post self-report surveys administered at baseline and post-intervention; post-intervention individual exit interviews (conducted via telephone or videoconference), and daily diary surveys and actigraphy assessments (sleep and physical activity) collected for 7 days within the 1-2 weeks before and after the intervention. All study surveys and daily diaries may be completed via REDCap, email, or paper mail, 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).

Pre-post survey measures*:*
The battery of self-report survey measures will be administered within approximately one week before and after the intervention. This battery will include the following validated self-report surveys: MAIA (body awareness) CAMS-R (attention regulation), EQ (cognitive decentering) DTS (distress tolerance), BVS (interoceptive bias), IUS-12 (ability to withstand uncertainty and ambiguity of future events), ASC (fear of recurrence), the ASI-3 (cardiac anxiety), the Consensus Sleep Diary, the PAVS (physical activity vital sign), Group Cohesiveness Scale, and the Program Satisfaction Survey. The baseline survey will also include questions on the patients' sociodemographic characteristics and medical history. Medical characteristics including SCAD characteristics (e.g., date, pregnancy associated), prior medical history, medical and psychiatric comorbidity, cardiac rehab attendance, and medication will be extracted for the participants' medical records. The pre-post survey battery is included in the IRB submission.

Daily Diary:
Participants will be asked to complete a daily diary of abbreviated survey measures for approx. 7 consecutive days during the 1-2 weeks before and after the intervention. To reduce survey burden, the daily diary will consist of 1-2 items from each of the pre-post survey measures; specifically, the items from that had the highest factor loading in the measure's validation study. The evening daily diary will include approx. 10 items. The morning daily diary will include approx. 20 items. In addition, to explore the acceptability of the daily diaries, there will be approx. 2-3 items asking about the experience of completing the daily diary itself (e.g., ease of completion, interference with daily activities). There will be a daily diary assessment each evening which includes items for all of the psychological variables and physical activity, and

there will be a 1-2 items diary assessing sleep quality each morning. Depending on the participant's preference, daily diaries can be completed via REDCap or emailed forms. The daily diary is included in the IRB submission.

Weekly home practice logs:
Participants will be given optional weekly home practice logs they can use to track their mindfulness practices throughout the week if they would like to. As part of the intervention, participants will be asked to complete approx. 15-20 minutes of mindfulness practice each day in between study sessions. Participants will be provided with optional weekly home practice logs they can use to record their experience if they would like to. Participants will not be required to submit the log to the study team. Depending on the participant's preference, home practice logs can be completed via REDCap or emailed forms. The home practice log is included in the IRB submission.

We will send participants audio recordings via a secure email link or Dropbox, to help with completing home practice.

Exit interview*:*
Upon completion of the intervention, participants will be asked to complete a 45-60 minute individual exit interview via phone or video conference. These interviews will be audio-recorded for transcription. The exit interview guide is included in the IRB submission.

Actigraphy:
An actigraphy device will be used to measure physical activity and sleep patterns. These devices are worn on the wrist. Participants will be asked to wear the actigraphy device daily for up to approximately 7 consecutive days during the 1-2 weeks before and after the intervention. The study team has a set of actigraphy devices which they have pilot tested for participant use in prior studies (Dana Farber Harvard Cancer Center IRB Protocol number 20-170). These devices will be mailed to participants along with detailed instructions (included in this submission) about when and how to wear the devices. Study participants will mail back the devices to the study team upon completion of data collection via return-stamped envelopes. Participants who do not mail back the devices will be sent a follow-up letter asking them to return the device, along with another pre-stamped envelope. All devices will be thoroughly disinfected by study staff between usages to prevent the spread of disease.

We will measure the following outcomes using the actigraphy device:

a. **Sleep** will be measured continuously for 7 days within the 1-2 weeks before and after the adapted MBCT intervention using actigraphy (wearable wrist device). We will evaluate wear compliance and calculate linear trends in total sleep duration, sleep efficiency, wake after sleep onset, and sleep onset latency over the course of the 8-week intervention (e.g., timings of sleep/awake, timings of being in bed).

b. **Physical activity** will be measured continuously for 7 days within the 1-2 weeks before and after the adapted MBCT intervention using actigraphy (GENEActiv wearable wrist device). We will evaluate wear compliance and calculate linear trends in moderate-vigorous physical activity, total steps, and sedentary time.

Measured Outcomes:
The primary outcomes are feasibility and acceptability of the intervention and research procedures. The exploratory outcomes are changes in psychological and behavioral variables, measured via pre-post intervention surveys, and daily diaries and actigraphy each day for 1-2

weeks before and after the intervention. Daily diaries will include psychological variables and self-reported physical activity (collected at night) and sleep outcomes (collected at morning). Covariates will be extracted from the medical record, including date of SCAD event, pregnancy-associated SCAD, medical and psychiatric comorbidities, cardiac rehab attendance, and hospital readmissions. Please refer to tables 1 and 2 below for details of feasibility and acceptability outcomes (Table 1) and exploratory outcomes (Table 2).

Table 1. PRIMARY OUTCOMES (Aims 1 and 2)	
Feasibility	
Enrollment	≥70% of eligible enroll; <20% ineligible due to each criterion; reasons for ineligibility; reasons for refusal; characteristics of refusers
Retention	≤20% participant attrition
Intervention components	≥70% session attendance; fidelity score ≥70%; ≤20% of sessions missed due to videoconference problems; ≤20% connections dropped during session; number (M≤2.0) and types of videoconference problems
Surveys	≥70% pre-intervention and post-intervention surveys completed; ≥70% daily diaries completed for 7 consecutive days; ≤20% missing data on daily diaries
Actigraphy	≥70% completed 7 consecutive days
Acceptability	
Intervention components	Program satisfaction (M≥7.0), ≥70% plan to use the skills, ≥70% would recommend the program to others (*post-survey);* likes, dislikes, suggestions for program improvement (*exit interview)*
Surveys	Ease of survey completion (1=not at all, 10=extremely M≥7.0); level of interference (1=not at all, 10=extremely M≤2.0; *post-survey*); experiences, challenges, suggestions for improvement (*exit interview)*
Actigraphy	Ease of actigraphy completion (1=not at all, 10=extremely M≥7.0; *post-survey*); experiences, challenges, suggestions (*exit interview)*

Table 2. EXPLORATORY OUTCOMES (Aim 3)		
Psychological Variables	**Measurement**	**Model Component**
Non-judgmental body awareness	Multidimensional Assessment of Interoceptive Awareness	Intervention mechanism
Attention regulation	Cognitive Affective Mindfulness Scale-Revised	Intervention mechanism
Cognitive de-centering	Experiences Questionnaire	Intervention mechanism
Distress tolerance	Distress Tolerance Scale	Intervention mechanism
Interoceptive bias	Body Vigilance Scale	FOR process
Intolerance of uncertainty	Intolerance of Uncertainty Scale	FOR process
FOR severity	Assessment of Survivor Concerns	FOR outcome
Cardiac anxiety	Anxiety sensitivity index 3	FOR outcome
Group cohesiveness	Group Cohesiveness Scale	Moderator
Program satisfaction	Program Satisfaction Survey	Moderator
Behavioral Variables	**Measurement**	**Model Component**
Sleep duration	Consensus Sleep Diary; Actigraphy	Health behavior outcome
Sleep efficiency	Consensus Sleep Diary; Actigraphy	Health behavior outcome
Sleep onset latency	Consensus Sleep Diary; Actigraphy	Health behavior outcome
Moderate-vigorous physical activity	Physical Activity Vital Sign; Actigraphy	Health behavior outcome
Total steps	Physical Activity Vital Sign; Actigraphy	Health behavior outcome
Sedentary time	Physical Activity Vital Sign; Actigraphy	Health behavior outcome
Note. All self-report measures are validated. Variables will be measured pre-post the 8-week intervention, and via daily diaries and actigraphy collected each day during the 1-2 week period before and after the intervention.		

Analysis Plan

For Aim 1 and Aim 2 will calculate frequencies and proportions and means and standard deviations (or medians and interquartile ranges if variables are non- normal) to assess feasibility and acceptability outcomes. T-tests or chi-square will be used to compare eligible patients who did and did not enroll, and those who enrolled and dropped out, on demographic and clinical variables. Exit interviews will be audio recorded, transcribed, and iteratively analyzed using

thematic content analysis in NVivo 11. Transcripts will be reviewed by two members of the study team to identify themes and develop a coding framework. Discrepancies in coding will then be resolved through discussion.

For Aim 3, we will examine frequency distributions for each exploratory outcome at each timepoint and use non-parametric tests if needed. We plan to use linear mixed effects models with repeated measures and an unstructured covariance matrix to assess changes over time for each psychological and behavioral variable (separate dependent variables. The predictor variables will be time (fixed effect: up to 16 levels across pre-post intervention surveys and daily diaries or actigraphy) and covariates relevant for each dependent variable (random effects). If there are any time effects, we will conduct follow up analyses to determine if those effects show a change over the course of the intervention period in the expected direction. We will create change scores (post-intervention survey minus pre-intervention survey) and explore correlations of changes in psychological variables with changes in behavioral variables. Missing data will be imputed using maximum likelihood estimation and, as a sensitivity analysis, the last observation carried forward. Given the exploratory nature of the proposed pilot study, we will focus the interpretation of Aim 3 analyses on effect sizes (Cohen's d) rather than statistical significance to assess potential signals for intervention effects.

For studies involving treatment or diagnosis, provide information about standard of care at Mass General Brigham (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.

All study participants will continue to receive standard care. The study procedures differ from standard care in that patients will be approached about the study and invited to participate. Those who are eligible and interested in participating will receive training in an evidence-based skills building program with their peers and a trained instructor. All patients who choose to participate in the study will continue to receive standard care with no other differences in their treatment beyond additional training in psychosocial skills. The alternative is to continue standard care without also participating in the study intervention.

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.

To minimize risks, all procedures will be performed in clinically stable participants who meet eligibility criteria. Participant risks are mitigated by excluding participants who are particularly vulnerable including those with severe mental illness, or those who are cognitively impaired, have short life expectancy. Participants will also be told that all participation is voluntary, and they can withdraw from the study at any time. Also, they will be told that the care they receive from their treating providers will in no way be affected by their participation or decision not to participate in this study.

Any serious adverse events (SAEs) will be reported to the IRB. SAEs will be collected and reported from screening to 30 days after the end of the study follow-up period for an individual participant. SAEs will be followed until resolution, stabilization, or until it is determined that study participation is not the cause.

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. 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 safety concern related to patients in this study is worsening psychological symptoms. Subject safety regarding psychological symptoms will be ensured per the protocol below.

The study therapist conducting the intervention session will be a trained clinician with a PhD in clinical psychology and expertise in the MBCT protocol. Thus, the study therapist will have expertise in assessment and treatment of mental health disorders and will be trained to identify if participants are experiencing severe psychological distress and can intervene if needed. 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. The interventionists will instruct patients at the start of the first session that if they experience worsening mood symptoms or concerns for their safety (e.g., suicidal thoughts) at any point during the study, they should let the interventionist, study staff, and/or their doctors know. At the start of the first session, we will (a) instruct participants that the group will be discussing emotional resiliency after SCAD and not medical details of SCAD, (b) instruct participants not to share personal details of their SCAD or relive their SCAD experience within the group, and (c) ask participants to share 1 positive coping skill they are using for their emotional well-being. The interventionist will interrupt any participants who overshare details of their SCAD and re-direct the discussion to positive coping. Participants will be instructed to call or email the research assistant (a) if they experience significant distress after the first session, or (b) if they experience any difficulties with the intervention throughout the study and would like an individual check in with the interventionist. In both cases the interventionist will call the patients for assessment and intervention if needed. Should a participant express suicidal ideation at any time during the study, the study clinician will immediately assess the subject and determine the appropriate course of action. Options for addressing suicidal ideation will include contacting the individual's treatment provider, referring for urgent (same day) evaluation and treatment in an outpatient clinic, or emergency room evaluation and hospitalization. Similar practices will be used for other emergencies, including but not limited to psychosis, homicidal or violent thoughts, or an acute change in a subject's physical status. The study PI (Dr. Luberto) and two of the study Co-Is (Drs. Hall and Park) are both licensed psychologist; Co-I Dr. Wood is a board-certified cardiologist. All of these members of the study team will be available to discuss and respond to concerns of participant safety over the course of the study.

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 PI 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 psychological 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).

To ensure the physical safety of participants, we will inform treating cardiologists that physical activity will be tracked as part of the study and obtain approval that it is safe for the participant to

be applying intervention skills to increased physical activity. Following guidelines from a 2018 AHA scientific statement on SCAD, we will advise SCAD patients in the trial to avoid prolonged high-intensity activities, highly competitive or contact sports, activities performed to exhaustion, abrupt increases in physical activity without warm-up, and exercising in extreme temperature.

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, and exit interview topics. 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.

While participants in this study may not directly benefit from their participation, we anticipate results from this study to benefit future research that seeks to reduce fear and improve health behaviors after SCAD. Participants may benefit from receiving the adapted MBCT intervention in terms of increase in mindfulness skills to cope with health-related fears, opportunity for peer support and clinician attention, and improvement in health behaviors.

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.

All adult subjects who satisfy the inclusion/exclusion criteria are eligible for enrollment in this study regardless of sex, race or ethnicity.

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 and most assessment measures have not been validated for use in non-English speaking populations.

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

https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb/Documents/Obtaining%20and%20Documenting%20Informed%20Consent%20of%20Non-English%20Speaking%20Subjects.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 via the MGH SCAD clinic through hospital flyers and cardiologist referrals. SCAD clinic cardiologists will obtain verbal permission from patients to share their information (e.g., name, phone number, MRN) with the study team. A member of the study team will then reach out to the patient to see if they are interested in participation. If the patient is not interested in study participation, study staff will discontinue contact. Patients will also be recruited through cardiologists' patient lists. The cardiologist and/or study staff will review the patient list for patients who have had SCAD in the past 3-18 months. Study staff will then send potentially eligible patients research invitation letters through Patient Gateway. Only patients who have agreed to be contacted about research studies will be sent a letter. We will use the required Research Invitation template (attached). Patients who proactively opt-out of the study will no longer be contacted. Patients recruited through hospital flyers may also contact the study team directly via phone or email, following the contact information on the flyer (e.g., study phone number and email address). The patient will be asked to provide the name of their cardiologist, who the study team will then contact to confirm the patient's history of SCAD, or the patient will be asked to give permission for study staff to review their electronic medical record to confirm a SCAD diagnosis.

Patients who are interested in study participation will be screened for eligibility over the phone 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 will include: confirmation of the patient's age (> 18 years old), SCAD diagnosis in past 3-18 months, internet access, ability to speak and read English, no terminal illness, no severe mental illness or past-year psychiatric hospitalization, no cognitive impairments preventing informed consent, ability to complete research procedures, and availability for planned session times. Confirmation will be based on the patient's verbal report, study staff's clinical judgment, and/or the patient's medical history. The RA will consult with the PI and/or review the patient's electronic medical record to confirm any questions about eligibility. 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.

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 Advarra Participant Payments System. Advarra 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 Advarra policy via the informed consent form. After agreeing to participate in the study, participants will also be asked to sign a "Advarra Participant Payment Card Acknowledgement of Receipt Form" 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 "Advarra Participant Payment Card Acknowledgement of Receipt Form" form 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 Advarra guidelines, and when ready will review and electronically sign the "Advarra Participant Payment Card Acknowledgement of Receipt Form" 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 Advarra acknowledgement forms will be stored in a locked, study cabinet.

Participants will be remunerated up to $50 via a reloadable debit card. Participants will receive $10 each for completing 80% of actigraphy days, 80% of daily diaries, the baseline survey, the post-intervention survey, and the exit interview.

For guidance, refer to the following Mass General Brigham policies:

Recruitment of Research Subjects

https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb/Documents/Recruitment%20of%20Research%20Subjects.pdf

Guidelines for Advertisements for Recruiting Subjects

https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb/Documents/Guidelines%20for%20Advertisements%20for%20Research%20Subjects.pdf

Remuneration for Research Subjects

https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb/Documents/Remuneration%20for%20Research%20Subjects.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 or via paper mail. The informed consent document will then be carefully reviewed with study staff via discussion with the patient either by phone or videoconference. Additionally, to ensure that patients understand what their participation will entail, they will be asked to reiterate in their own words the purpose of the research, what they will need to do as participants in the study, and what the potential risks, potential benefits, and alternatives are. After the form is reviewed by both study staff and the patient and all of the patient's questions have been answered, the patient may then sign and submit the form electronically or via paper mail. 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 two ways, depending on patient preference: 1) electronically (via REDCap or emailed pdf of the consent form) or 2) via paper mail correspondence. Patients who opt to receive the consent materials via paper mail will be asked to provide a mailing address. Patients 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):
Patients will be emailed the informed consent portal via REDCap. The REDCap link will connect the patient to an encrypted REDCap portal; the Electronic/Paperless Consent (EIC) Template Project will be used. Once the patient 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 patient, through the consent discussion with study staff over the phone. The patient will be given ample opportunity to ask questions and take their time to consider their participation. If a patient 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, patients will digitally sign and date/time the consent form. Additionally, the patient 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 patient 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. MGB 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 patient 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 patient, study staff will mail 2 signed copies of the informed consent form for the patient 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.

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 Mass General Brigham IRB website:
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb

For guidance, refer to the following Mass General Brigham policy:
Informed Consent of Research Subjects:

https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb/Documents/Informed%20Consent%20of%20Research%20Subjects.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 Study Principal Investigator, Dr. Luberto (licensed clinical psychologist), will be responsible for ensuring participants' safety on a daily basis. She will be assisted in this responsibility by Dr. Park (licensed clinical psychologist) and Dr. Wood (board-certified cardiologist), and the clinical research coordinator. Together, they will be responsible for monitoring participant safety, evaluating the progress of the study, reviewing procedures for maintaining the confidentiality of data, the quality of data collection, management, and analyses.

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 Mass General Brigham IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Mass General Brigham 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 Mass General Brigham IRB 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.

For guidance, refer to the following Mass General Brigham policies:

Data and Safety Monitoring Plans and Quality Assurance
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb/Documents/Data%20and%20Safety%20Monitoring%20Plan%20in%20Human%20Subject%20Research.pdf

Reporting Unanticipated Problems (including Adverse Events)
https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb/Documents/Reporting%20Unanticipated%20Problems%20including%20Adverse%20Events.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 MASS GENERAL BRIGHAM

Specimens or data collected by Mass General Brigham investigators will be sent to research collaborators outside Mass General Brigham, 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.

Data collected from the current study will not be sent to research collaborators outside of Partners.

Specifically address whether specimens/data will be stored at collaborating sites outside Mass General Brigham 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.

Data will not be stored at collaborating sites outside of Partners for future use not described in this protocol.

RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE MASS GENERAL BRIGHAM

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

Data will not be collected by research collaborators outside of Partners.