A Randomized Controlled Trial to Reduce Hopelessness through Enhanced Physical Activity in Adults with Ischemic Heart Disease

Study Protocol and Statistical Analysis Plan

NCT03907891

December 14, 2018

Study Protocol

Recruitment, Consent and Screening. Nurse recruiters, who are employed by the hospital's Research Department and who do not provide direct patient care, will determine eligibility for hopelessness screening by reviewing the patient's medical record. Nurse recruiters will approach eligible hospitalized IHD patients and invite them to be screened for potential consideration for the study. Recruiters will use a script to introduce the screening portion of the study, explaining that eligibility for the RCT will depend on screening results. Interested patients will provide written consent for the hopelessness screening, including a HIPAA waiver. The consent will include permission for review of the patient's medical records to collect patient characteristics. These data can contribute to external validity of the study findings. Patients will be screened for hopelessness using the 10-item state subscale of the 23-item State-Trait Hopelessness Scale (STHS). Based on cut-point criteria in our earlier research, a criterion of ≥1.8 will be used for classification of moderate to severe hopelessness levels. Patients who do not meet the hopelessness criteria will be thanked for their participation.

We will enroll both women and men. Our recent pilot enrolled 30 participants and 9 were female (30%), which is typical for the IHD population. We expect to experience enrollment and retention of women at a rate equal to our pilot work, since we are using the same recruitment strategies. We will recruit patients of all races and ethnicities. Our recent pilot enrolled 30 participants and 3 were racial/ethnic minority (10%). However, we expect our sample to be representative of the hospital's catchment area (different from the pilot study hospital), which has 15% racial minority. If needed, we will oversample for women and minorities to enroll a heterogeneous sample congruent with the American population. We will ensure the recruitment of women and racial minorities by training the nurse recruiters and other staff.

Study Consent and Randomization. For patients who meet hopelessness screening criteria and wish to participate, the recruiters will read through a script to describe the RCT. Recruiters will explain that if a patient enrolls, there is a 33% chance of being in one of the three groups (MSS, MSS with SOS, or AC). Patients will be informed that if they are randomized to the MSS with SOS group, they will be asked to identify a significant other to provide support as part of the study. If the patient agrees to enrollment in the study, written consent will be obtained and the patient will be immediately randomized using a randomization scheme loaded into the UIC Biomedical Research Informatics Core's (BRIC's) Research Electronic Data Capture (REDCap) system. Patients in the MSS with SOS group will then be asked to select a family member or friend to serve as their support person. The nurse recruiter will meet with the significant other in the hospital, if available, or collect the contact information for the significant other from the patient and contact the significant other by phone. The nurse recruiter will explain the study to the significant other and the role that s/he would play in sending text messages (developed by the researchers) to the patient. If the significant other agrees, the nurse will either provide the consent form to the significant other during the patient's hospitalization or mail a consent form to the significant other and provide a postage-paid envelope for its return. The timing of the text

messages coincides with the typical 6 to 8 week recovery period for patients who have experienced MI or CABG, a time when family members and friends wish to be helpful. All (100%) of the patient's significant others invited to participate in our pilot RCT were willing to do so. However, in the proposed full RCT, if a significant other does not wish to participate, the patient will be asked to select a different significant other and that person will be contacted.

Data Collection. Data collection for all three groups will occur in the patient's home at 3 time points over the 24-week period and will include accelerometer monitoring for 1 week prior to each of the data collection visits. There will be one accelerometer placement visit in the patient's home at baseline (within 1 week of hospital discharge). At the one-time accelerometer visit, the data collector will instruct the patient on the use of the accelerometer and PA log, place the monitor on the patient, and activate it. This visit will take approximately 15 minutes. The patient will be asked to wear the accelerometer and complete the PA log for 1 week. The data collector will return after the week to retrieve the accelerometer and to conduct baseline data collection. At weeks 7 and 23, the accelerometer will be shipped to the patient with instructions to wear it again for 1 week. At weeks 8 and 24, data collectors will return to the patient's home to retrieve the accelerometer and to conduct data collection. All data collection interviews will take on average 30 minutes. If a patient becomes fatigued during any home visits, s/he will be allowed to rest or the study staff will return the following day to complete the session. All patients in our preliminary study completed each of the accelerometer visits and data collection interviews in one sitting and none complained of fatigue. Medical record data will be collected after the patient's hospital discharge.

Description of the Intervention. Intervention components include a 60-minute motivational interviewing session with a nurse and text messages (developed by researchers) sent from the nurse for the MSS and MSS with SOS groups. Patients in the MSS with SOS group will also receive text messages (developed by researchers) sent by the significant other. The AC group will receive 60 minutes of AHA videos with instruction on taking their radial pulse (details below). Intervention components for the 3 groups include:

Group 1: MSS. Patients will receive a 60-minute session of motivational interviewing in their home from a trained nurse. Motivational interviewing, a directive, client-centered counseling style for eliciting behavior change by helping clients to explore and resolve ambivalence, has been effective in increasing PA in patients with multiple sclerosis, stroke, and IHD. The nurse will apply motivational interviewing techniques to explore the patient's thoughts about making a behavior change to attain adequate PA. The session will include the patient's thoughts about PA, types of PA available, barriers to PA, the benefits of PA, and setting PA goals. Because of a hopeless patient's negative and helpless outlook on the future, the motivational interviewing sessions will be tailored with an increased emphasis on the benefits of PA, overcoming barriers to PA, and the patient's confidence level in achieving PA. Two motivational interviewing tools (measured on a Likert-type scale) will be used to help patients think about PA in a concrete manner: 1) an "Importance of PA" ruler and 2) a "Confidence with PA" ruler. Patients will be encouraged to exercise based on instructions provided by the hospital staff. The nurse will provide a written copy of the hospital PA instructions and a PA log. The patient's ability to take their radial pulse before and after PA will be assessed, and patients will be provided written

instructions on the correct manner to take a radial pulse. Patients will be provided with 3 motivational magnets with the Heart Up! logo to be used for displaying the PA log and rulers.

After the motivational interviewing is complete, the nurse will inform the patient of the start date of the nurse's text messages. Patients will receive daily motivational text messages from the nurse for 6 weeks. The 42 text messages were developed by the research team based on Self-Determination Theory and Cohen's Stress and Coping Social Support Theory. As in our preliminary work, the texts will be sent via the REDCap automated system. The order of texts will be randomized so that the order is unique to each patient, allowing for us to determine if the text messages are effective in general (versus the order that that messages are given). Based on preferences expressed by patients in our earlier work, texts will also be randomized to arrive within a 2-hour time frame from 10:00 am to 12:00 noon. The automated system confirms that texts were sent. The motivational interviewer nurse will confirm by phone that the patient receives her/his first text from the REDCap system. Although REDCap cannot track whether texts were opened/read, patients will be asked to track the number of text messages from the nurse that they read over the 6-week period using a log provided by the nurse.

Group 2: MSS with SOS. Patients will also receive a 60-minute session of motivational interviewing in their home from a trained nurse and text messages from a nurse for 6 weeks, as described above. In addition, patients will receive daily text messages from their significant other for 6 weeks. It is hypothesized that the Heart Up! intervention's integration of social support within the patient's existing social network (the patient's self-identified significant other) will be a critical component and provide the greatest impact in increasing PA in hopeless patients. Researchers developed the 42 significant other text messages based on Self-Determination Theory and Cohen's Stress and Coping Social Support Theory. The motivational interviewing nurse will provide the text messages to the significant other in writing (mailed with the consent). The order of texts sent from the significant other will be randomized so that we can determine their effectiveness in general. The significant other will be asked to type and send the text message listed for each date to both the patient and to the REDCap system (for verification that the message was sent). Based on feedback received from patients in our pilot study, and to avoid text messages being sent at the same time as the nurse text messages, significant others will be asked to send their text messages between the hours of 1:00 pm to 3:00 pm and to vary the times sent from day to day. If the REDCap system does not receive a copied text from the significant other by 3:00 pm, it will send a reminder to the significant other. The motivational interviewer will confirm by phone that the patient received the first text from the significant other. Patients will be asked to track the number of text messages from the significant other that they read over the 6-week period using the log provided. Our dyadic approach is distinctive in combining these two components (motivational interviewing and text messaging) by the nurse with the additional unique component of an emotional support text messages from the patient's significant other, for use exclusively with hopeless IHD patients. Because the Heart Up! intervention includes only 1 motivational interviewing session (followed by text messages by a nurse and significant other), Heart Up! has good potential to be translated into practice with hopeless IHD patients in an efficient and practical way.

Group 3: AC. Patients in the AC group will receive a 60-minutes session with a research assistant focused on the viewing of AHA “About Conditions” and “Tips for Healthy Living” YouTube videos. The research assistant will additionally provide a written copy of the hospital PA instructions, will assess the patient’s ability to take their pulse, and provide written instructions on the correct manner to take a radial pulse.

Patients in all 3 groups will have interaction with data collectors in their home for the first accelerometer placement and 3 data collection visits. The motivational interviewer or data collector (for the AC group) will ask permission of patients to audiotape the motivational interviewing or AHA video session for quality assurance purposes.

Treatment Fidelity. Treatment fidelity will be assured through established methods outlined by the Treatment Fidelity Workgroup of the NIH Behavior Change Consortium. A treatment fidelity plan was developed by the PI as part of the preliminary study and will be carried out in the proposed RCT by the project manager, in collaboration with the PI. The plan incorporates the workgroup’s 5 recommended components: study design, training, treatment delivery, treatment receipt, and treatment enactment. Every 3 months, 15% of the audiotaped motivational interviewing sessions will be randomly selected for QA review. Tools completed by patients as part of the intervention (i.e. rulers, PA log, and text messaging log) will undergo QA review for completeness and accuracy.

Incentives. To compensate patients for the time taken and any inconvenience for home visits and accelerometer monitoring over the 6-month study period, we will compensate $20 for completion of the baseline data collection, $30 after week 8, and $50 after week 24 (total $100). At study completion, all patients will receive a thank you letter and patients in the AC group will receive the Heart Up! motivational magnets (given previously to patients in the MSS and MSS with SOS groups).

Attrition. The data collectors and motivational interviewers will document attrition, including dates and reasons, during reminder telephone calls with patients, calls to significant others, and visits to patients. Recruiters, data collectors, and motivational interviewers will emphasize the importance of completing the intervention, wearing the accelerometer, and completing the 3 data collection sessions. Patients will be scheduled for their first home visit and provided an appointment card for this visit prior to hospital discharge. Patients will also receive reminder phone calls for all appointments. The motivational interviewer will call the patient and significant other (if appropriate) to confirm that text messages are being sent and received. Patients will be provided adequate time for discussion and to have their questions answered. Study participants will be provided with a toll-free number to call the study office with any questions. These strategies were effective in our pilot study, in which 67% of patients and 100% of significant others completed the study.[19]

Statistical Analysis Plan

Data Management. Data will be stored on a secure dedicated server with appropriate firewalls using the UIC REDCap system (see Data and Safety Monitoring Plan). Data will be entered into the REDCap database via Web interface. The web server synchronizes uploaded files to an alternate location and is backed up daily. De-identified data sets for analyses will be created by

importing data from REDCap into the statistical program R. Quarterly QA reports will be reviewed by a Data and Safety Monitoring Committee.

Plan for Statistical Analyses. The rigor of the study design will produce objective, unbiased, and interpretable results. Data analysis and hypothesis testing will proceed in several steps: 1) description of the sample overall and across the 3 treatment groups, as well as patients lost to attrition; 2) confirmation of internal reliability of scales; and 3) bivariate and multivariate analysis of the interrelationships between treatment groups for PA and state hopelessness.

Analysis plan for Aim 1 and 2. **Aim 1**: Test the effectiveness of 6 weeks of MSS and MSS with SOS on increasing mean minutes per day of moderate to vigorous PA, measured by an ActiGraph accelerometer and **Aim 2**:Determine the effects of change in minutes per day of moderate to vigorous PA on state hopelessness, measured by the State-Trait Hopelessness Scale (STHS). Initial bivariate analyses for Aims 1 and 2 will be conducted using ANOVA or simple linear models using R, testing for changes in minutes of moderate to vigorous PA (Aim 1) or association between change in exercise and changes in state hopelessness (Aim 2) between baseline and week 8 or baseline and week 24 by treatment group. We will also use linear mixed effects models (lme4 function in R) to incorporate multiple waves of data from each participant, covariates, and mediators into the analysis (Aims 1, 2 and 3), following the general approach we have used before. In particular, we will simultaneously model data across the two post-baseline time points and account for within- and between-subject effects and time-independent and time-dependent predictors. For Aim 1, we will predict minutes of moderate to vigorous PA by treatment group, adjusting for covariates and baseline activity level. Aim 2 follows an approach similar to Aim 1, and predicts state hopelessness levels by changes in exercise, adjusting for covariates and baseline state hopelessness levels.

Analysis plan for Aim 3. **Aim 3:** Determine if social support (measured by the ENRICHD Social Support Inventory) and motivation (measured by the Exercise Self-Regulation Questionnaire) mediate effects of the Heart Up! intervention on PA. For Aim 3, models for Aims 1 and 2 will be expanded by also including one or more mediating variables, including prior measurements of state hopelessness and moderate to vigorous PA, using the three-step approach of Barron and Kenney: 1) Confirm relationship between treatment and social support or motivation using a linear mixed model, 2) Confirm relationship between treatment and changes in exercise (Aim 1), and 3) Predict changes in exercise by both treatment and social support (or motivation) demonstrating that social support and/or motivation explain most of the changes in exercise as compared to treatment. Models will include covariates as in Aims 1 and 2 and include multiple waves of data. We will use a modified Bonferroni approach to control for Type I errors when testing multiple mediators simultaneously.

Subgroup analyses (e.g. sex- see section 3C.20) will be conducted by estimating main effects of treatment groups or mediating variables on the response within each subgroup, and testing for potential differential effects between subgroups by incorporating relevant interaction terms into the models.