In Person and mHealth Coping Skills Training for Symptom Management and Steps in Stem Cell Transplant Patients

NCT03859765

May 23, 2022

Purpose of the Study

Our group developed a mHealth pain coping skills training program for HCT patients and found in a small pilot trial (R21) that improved pain coping led to increased daily activity and reduced physical disability. However, fatigue and distress were also barriers to physical activity. **We propose to develop a novel mHealth behavioral intervention to enable HCT patients to effectively cope with symptoms to improve their ability to engage in physical activity that can improve physical disability.** Our interdisciplinary team (psychiatry, hematology/oncology, occupational therapy) will develop a hybrid in-person and mHealth HCT Coping Skills Training for Symptom Management and Daily Steps (HCT Symptoms and Steps) intervention protocol. HCT Symptoms and Steps will provide patients with coping skills training and activity coaching sessions to enhance their ability to cope with symptoms that interfere with activity. HCT Symptoms and Steps will be developed by experts in symptom management, members of the HCT medical team, and with extensive input from HCT patients. Innovative features to be considered include: initial in-person sessions with subsequent sessions via video-conferencing at home; a mobile application and wireless activity trackers to capture symptoms and activity data for real-time personalized feedback; cognitive behavioral strategies to decrease the impact of symptoms – pain, fatigue, distress – that most interfere with activity.

Aim 1: Develop the HCT Symptoms and Steps protocol for HCT patients. Development will consist of 5 focus groups with HCT patients (n=6/group), a focus group with HCT providers (N=6), and user testing with 10 HCT patients. **H1:** This process will develop a feasible and acceptable protocol for HCT patients with pain, fatigue, and distress.

Aim 2: Use a small randomized controlled trial (N=40) to examine feasibility and acceptability of the developed HCT Symptoms and Steps protocol. Feasibility will be assessed via (a) study accrual, (b) protocol adherence, and (c) retention. **H2:** Feasibility will be determined by accrual (N=40/12 months), ≥80% adherence to the protocol, and ≤20% attrition. Acceptability will be demonstrated by 80% of participants reporting intervention satisfaction.

Aim 3: Examine outcome patterns suggesting the efficacy of the HCT Symptoms and Steps protocol for improving physical disability and other outcomes compared to an HCT Education group. **H3:** Between-group effect sizes will be used to evaluate patterns suggesting intervention efficacy on measures of physical disability (self-report, 6-min walk test), pain, fatigue, distress, physical activity (daily steps), and self-efficacy for symptom management.

Confirmed hypotheses would provide the first demonstration of the feasibility, acceptability, and positive impact of a hybrid in-person and mHealth coping skills training and activity coaching intervention that reduces physical disability by concurrently and synergistically decreasing symptom burden and increasing physical activity. This project has the potential to lead to future research (R01) that can redesign existing modes of behavioral intervention delivery, improve continuity and coordination of care, and ultimately enhance patient outcomes.

Background & Significance

- Should support the scientific aims of the research

Background & Significance

Hematopoietic stem cell transplant (HCT) is an aggressive treatment for life-threatening cancers. HCT has led to improved prognosis and survival, but 70-80% of HCT patients experience significant physical disability, which is exacerbated by persistent symptoms.[1,2] Pain, fatigue, and psychological distress are among the most prevalent and debilitating symptoms for HCT patients. Higher pain, fatigue, and distress in HCT patients are associated with greater physical disability and difficulty adhering to physical activity guidelines.[1,3-11] Research shows HCT patients experience a significant increase in physical disability as their pain, fatigue, and distress increase.[1,2] This physical disability along with their symptom burden interferes with patients' ability to engage in recommended physical activity that can improve disability, symptoms, and other important health outcomes.

Perhaps paradoxically, physical activity is the most common way to reduce physical disability. Physical activity is a part of standard care guidelines following transplant; HCT patients are instructed to engage in 30 minutes of daily activity or 2700 steps.[12] Research shows that physical activity leads to reduced disability and other important health outcomes, including reduced symptom severity and increased psychological functioning.[9,13-18] Increasing evidence shows physical activity is safe and feasible for HCT patients, can alleviate symptoms and side effects of treatment, and can improve quality of life and potentially survival.[19-23]

Despite the recommendations and its many benefits, HCT patients report difficulty engaging in physical activity. Pain, fatigue, and distress are major barriers to physical activity.[2,19,24] HCT patients report increased severity of symptoms when they attempt to follow activity guidelines; thus, symptoms either limit their activity or stop it completely.[19] Low levels of activity exacerbate disability, and can result in impaired cardiorespiratory fitness and decreased mobility, strength, and endurance.[18,23] Low levels of activity also increase patients' risk for chronic diseases and may ultimately negatively impact survival.[18,23] Teaching HCT patients to cope with symptoms and engage in activity is critical to helping them increase activity and reduce disability.

Cognitive behavioral coping skills training interventions are an efficacious treatment for cancer-related symptoms. Traditional analgesic and other medications for pain and symptom management have limitations, particularly in HCT patients. Some analgesics and corticosteroids are contraindicated[25] and others can only be given orally. Importantly, medications often do not fully relieve pain, fatigue, and distress, and patients report significant side effects.[26] Cognitive and behavioral factors play an important role in patients' ability to cope with symptoms and engage in physical activity.[27-29] HCT patients with persistent symptoms are likely to have low confidence in their ability to control their symptoms (i.e., self-efficacy for symptom management). HCT patients in our past work who have low self-efficacy for managing symptoms are more likely to experience problems with symptoms, adherence to activity recommendations, and physical disability.[30,31] Work in other patients with persistent symptoms has found cognitive behavioral coping skills training protocols are efficacious in reducing symptom severity and improving self-efficacy for symptom management, physical activity and physical disability.[32-36] However, the application of these protocols to HCT patients is limited by in person sessions, delivery of sessions in a medical center setting, and/or lack of tailoring to HCT patients' specific needs.[37,38]

Physical disability and persistent symptoms (pain, fatigue, distress) complicate an already challenging recovery course.[8,39] HCT patients spend pre- and post-transplant days as

inpatients, have weeks of intensive outpatient care, and then return home often many miles from the hospital. HCT patients return home with compromised immune functioning, low vigor, and restriction on normal activities (e.g., driving, cooking, yard work, church) that could increase infection risk or compromise safety. HCT patients report feeling socially isolated and disconnected from their medical team. HCT patients experience these challenges during a critical time of transition from hospitalization to home. Mobile health (mHealth) technologies can improve and extend intervention strategies during this time of transition. A protocol that uses mHealth technology for delivery may be particularly beneficial for HCT patients as it allows the medical team to provide care to the patient in his /her home. The patient remains connected to the medical team during an important time of transition, which can increase continuity of care and access to treatment, and decrease patient burden.

We aim to develop and test a combined coping skills training and activity coaching protocol that: first, is feasible and acceptable, and second, improves physical disability, as well as pain, fatigue, distress, and physical activity in HCT patients. We have used the NIH Treatment Development Stage Model[40] to inform the research activities and design. This study focuses on development (i.e., focus groups, user testing) and a small pilot trial (Stage I), with emphasis on the mHealth component and mobile app. Data gathered from research activities will inform protocol modification and study results will be used to prepare for Stage II (efficacy trial). As described in *Preliminary Studies*, the proposed interdisciplinary research team is uniquely positioned to develop and test a coping skills training for symptom management and activity coaching protocol.

We propose a novel intervention protocol that uses a hybrid in-person and mHealth intervention delivery model. The use of mHealth technology to deliver the proposed intervention is likely to be more effective than traditional interventions delivered in-person only, improving patient access to the intervention by decreasing burden. The NIH recently stated that the future of patient care should use a hybrid model of face-to-face contact integrated with remote strategies to provide balance between technology and the "human touch." The proposed innovative intervention addresses these recommendations (i.e., in-person and mHealth strategies). We have piloted hybrid work and the proposed project is a natural extension as we increase face-to-face contact, increase mHealth technology, and address shortcomings of the previous protocol (we now address pain, fatigue and distress, and incorporate activity coaching). Our past protocol included 1 in-person session at the hospital between patient and therapist, which led to development of a successful working relationship and integration of the intervention with the patient's medical care.[31] Then, once the patient returned home, 5 sessions were conducted via video-conferencing. This bridge between hospitalization and home maintained continuity of care. This work demonstrated that a mixed delivery modality fostered a strong patient-therapist relationship that likely increased feasibility, acceptability, and efficacy of the intervention.[31] Further, our experience with mHealth technology suggests video-conferencing is human touch as it mirrors in-person sessions and is interactive and personal. Traditional coping skills training interventions have been delivered almost exclusively in-person in major medical centers. For HCT patients, travel is burdensome due to significant symptom burden and strict activity restrictions. Distance from medical centers is a concern for several communities in the US and mHealth interventions can increase access to care. An intervention that begins in-person immediately following transplant and continues via mHealth technology increases access by reducing travel barriers for a cancer population that experiences significant burden.

*Due to COVID-19, we propose a **temporary** amendment. Session 1-3 will now be conducted via telephone or video-conferencing, the same way as the approved session 4-7.

Design & Procedures

- Describe the study, providing detail regarding the study intervention (drug, device, physical procedures, manipulation of the subject or the subject's environment, etc.). Discuss justifications for placebo control, discontinuation or delay of standard therapies, and washout periods if applicable. Identify procedures, tests and interventions performed exclusively for research purposes or more frequently than standard of care. Include alternative therapies, concurrent therapies discontinued per protocol, risk benefit ratio, and use of tissue/specimens. Discuss monitoring during washout periods if applicable. Include brief description of follow-up, if any.

Study Overview. We will develop and test an in-person and mHealth HCT Coping Skills Training for Symptom Management and Daily Steps (HCT Symptoms and Steps) intervention protocol. To do this, we will develop a mobile app, conduct focus groups, complete user testing, and conduct a small RCT to examine feasibility, acceptability, and outcome patterns suggesting intervention efficacy.

Methodological Features. This protocol has several important methodological features. First, we will combine symptom management and activity coaching to address the multiple recovery challenges faced by HCT patients. Second, we will use in-person and video-conferencing sessions to bridge hospitalization and home. The initial HCT Symptoms and Steps coping skill (1) and activity coaching (2) sessions will be in-person in the hospital which provides several benefits including: integration of HCT Symptoms and Steps into patients' medical care; facilitation of a relationship between therapist and patient; and, establishment of care that bridges hospitalization and home. All sessions following the initial in-person sessions will be delivered to the patient in his/her home through video-conferencing. The use of video-conferencing (vs. in-person or phone) is likely to provide important advantages. A) HCT patients often live many miles from the hospital and are advised against extended travel thus video-conferencing will increase intervention access. B) Empirical work suggests educational and psychosocial content is better communicated through video-conferencing than by phone.[41] C) Video-conferencing may enhance factors suggested by social cognitive theory to impact self-efficacy for symptom management: *mast ery*, enhanced by practice/feedback in the home environment; *vicarious learning*, enhanced by therapist and video clip modeling; *verbal encouragement*, personalized to the patient's home skills practice; and, *observation of* and *addressing negative physiological and affective responses* to skills use in the patient's practice environment. Third, a mobile app will provide HCT Symptoms and Steps participants with accessible coping skill content (audio and video), data syncing of daily steps from their wireless activity tracker, daily assessment of symptoms and activity, and real-time personalized feedback (push notification) based on symptoms and steps. The mobile app will be accessible on study iPhones and/or personal tablets/smart phones. Fourth, we have incorporated an objective assessment of physical disability (6-min walk test).

HCT Symptoms and Steps Intervention Mobile App Development. The study team (Kelleher, Somers, Sung) responsible for mobile app development have worked together for several years and will be ready to immediately begin app development in Year 1.[30,31,42] We propose that the HCT Symptoms and Steps app include: 1) patient content on coping skills and physical activity (e.g., audio, skills demonstration videos), 2) syncing of wireless activity tracker data and transmitting in real-time to study staff, 3) coping skills use tracking, 4) daily symptoms assessment, 5) push notifications from the therapist (3x/week) that include reminders, encouragement, and real-time personalized feedback based on coping skills use and symptoms assessment, and 5) a link to the intervention video-conferencing application. We will use feedback from the focus groups and user testing (see below) to make revisions to the mobile app as indicated. Pattern Health (Durham, NC) is a digital health company specializing in patient-centered web and mobile products for clinical and medical research

and health data tracking and analysis, with expertise working with wireless devices and improving patient engagement. Pattern Health has an established relationship with researchers at Duke and will be contracted for the development of a mobile app for use in the current study (see letter of support). The investigators have already been working with expert technicians at Pattern Health and will continue to work closely to design and develop the study app.

Focus Groups/User Testing. We will conduct focus groups and user testing to iteratively develop the HCT Symptoms and Steps protocol. Focus groups will be sequential allowing for the data from each group to iteratively update the protocol prior to the next group. In focus groups, patients will respond freely to verbal feedback based on the presentation and questioning, and provide written responses to assessments of needs, barriers, mobile app format preferences, and ratings of app and material helpfulness and ease of use. Focus groups will be audio-recorded. Focus group and user testing participants will be 40 patients who have undergone HCT and 6 healthcare providers from the Adult Blood and Marrow Transplant (ABMT) Clinic.

Randomized Controlled Trial. We will use a small RCT to assess the feasibility, acceptability, and outcome patterns suggesting efficacy of a HCT Coping Skills Training for Symptom Management and Daily Steps (HCT Symptoms and Steps) protocol. This study will be conducted in the ABMT Clinic with 40 HCT patients. Following consent (consent process detailed below), participants will be randomly assigned in equal allocation to one of two conditions: 1) HCT Symptoms and Steps or 2) HCT Education. HCT Symptoms and Steps will provide patients with cognitive behavioral coping skills training and activity coaching sessions to enhance their ability to manage symptoms that interfere with activity. All participants will receive a wireless activity tracker (Fitbit) to track steps; Fitbits will not be returned, participants will keep their Fitbit. All participants who do not have a smart phone will be lent one (iPhone) equipped with Internet access to access the mHealth features: video-conferencing, coping skill content, activity tracker syncing, daily symptoms assessment, and personalized feedback (via push notification) based on symptom and step data. HCT Education will only have access to activity tracker syncing and daily symptoms assessment. HCT education participants will be encouraged to download the Transplant (HCT) Guidelines mobile app that is free of charge. The Transplant Guidelines app is developed by the National Marrow Donor Program and designed for HCT patients with a focus on treatment guidelines for patients before and after transplant. The Transplant Guidelines App provides recommended annual check-up guidelines and timing and contains helpful information, checklists and reminders for patients who have had a blood or marrow transplant. App content also includes cancer education, information about health and well-being, cancer treatment guidelines specific to HCT patients, and what to expect at follow-up visits. App features allow participants to use a GvHD symptom checker to help identify early signs of GvHD and make notes, e-mail guidelines and symptom checker results to self, and set reminders for appointments, medications, and exercise. All participants will complete 2 assessments: pre-treatment and post-treatment. We will recruit 10 patients per quarter (3-4/month) to complete the recruitment goal of 40. Participants will receive $20 for completing each assessment. **Therapist Training.** Coping skills training sessions will be delivered by a doctoral level psychologist with experience delivering cognitive behavioral interventions. Activity coaching sessions will be delivered by an OT with expertise working with HCT patients. Treatment strategies will be taught through didactic instruction, audio-/video-recorded illustration of techniques, and role-play. **Procedures to Ensure Consistency of Treatment.** To ensure consistency with the intervention protocol: 1) therapists will follow a treatment manual, 2) weekly supervision will occur, 3) sessions will be audio-recorded and reviewed during supervision and feedback provided, and 4) ratings of treatment adherence and competence will be conducted.

For individuals who already have a smartphone, they will use their own device. For participants who can use their own phones, the following steps will be taken to ensure the phones are secured: 1) We will enable encryption on the device and verify that data protection is enabled, set "require passcode" to immediately, and enable erase data to "automatically erase the device" after 10 failed passcode attempts. 2) We will set Auto-Lock.

For participants who have their own smart phone with a Fitbit app installed/personal Fitbit account already created, we will loan them a study phone for the purposes of study participation to access their study Fitbit account which will not include any personal identifiers. This measure is taken for these individuals as another layer of security.

*Due to COVID-19, we propose a **temporary** amendment. Participants will now be screened and must have a smartphone to be eligible. We will be temporarily suspending giving participants smartphones and FitBits.

Selection of Subjects

- List inclusion/exclusion criteria and how subjects will be identified.

1. *Patients who have undergone hematopoietic stem cell transplant (HCT) due to an oncological disease* (e. g., leukemia, lymphoma, multiple myeloma) (up to N=30) from the Adult Blood and Marrow Transplant (ABMT) Clinic at Duke Cancer Institute will be recruited to participate in 5 focus groups (about 6 participants in each group). Eligibility criteria include: 1) being at least 18 years old, 2) report clinical pain, fatigue, or psychological distress, at least 2/3 symptoms with 1 symptom rating at a 3 or greater on a scale from 0-10 and 1 symptom at any level, and 3) life expectancy at least 12 months. Exclusion criteria include: 1) cognitive impairment (e.g., dementia) recorded in the chart or suspected by healthcare provider, 2) presence of a severe psychiatric condition (i.e., psychotic disorder or episode) or a psychiatric condition (e.g., suicidal intent) that would contraindicate safe participation in the study as indicated by the medical chart, treating oncologist, or interactions with the medical/study staff, and 3) inability to converse in English. These focus groups are designed to facilitate development of a feasible and acceptable CST Step-Up intervention protocol by using rigorous qualitative (focus groups) and quantitative (self-report) methods.

2. *Healthcare providers (about N=6)* will participate in 1 focus group. Healthcare provider participants will include oncologists, oncology nurse practitioners, oncology physicians' assistants, and oncology nurses. These focus groups are designed to facilitate development of a feasible and acceptable CST Step-Up intervention protocol by using rigorous qualitative (focus groups) methods.

3. *Patients who have undergone hematopoietic stem cell transplant (HCT) due to an oncological disease* (e. g., leukemia, lymphoma, multiple myeloma) (up to N=10) from the Adult Blood and Marrow Transplant (ABMT) Clinic at Duke Cancer Institute will be recruited to participate in user testing of the developed CST Step-Up protocol. Eligibility criteria include: 1) being at least 18 years old, 2) report of clinical pain, fatigue, and psychological distress, and 3) life expectancy at least 12 months. Exclusion criteria include: 1) cognitive impairment (e.g., dementia) recorded in the chart or suspected by healthcare provider, 2) presence of a severe psychiatric condition (i.e., psychotic disorder or episode) or a psychiatric condition (e. g., suicidal intent) that would contraindicate safe participation in the study as indicated by the medical chart, treating oncologist, or interactions with the medical/study staff, and 3) inability to converse in English. User testers will complete the developed CST Step-Up protocol and provide feedback following each session. The qualitative and quantitative data gathered from user testing will be used to refine the CST Step-Up intervention protocol.

Randomized Controlled Trial. We will use a small RCT to assess the feasibility, acceptability, and outcome patterns suggesting efficacy of the fully developed HCT Coping Skills Training for Symptom Management and Daily Steps (CST Step-Up) protocol. This study will be conducted in the Adult Blood and Marrow Transplant (ABMT) Clinic and involve 40 HCT patients. Inclusion criteria: 1) HCT due to oncological disease, 2) age $\geq$18, 3) report clinical pain, fatigue, or psychological distress, at least 2/3 symptoms with 1 symptom rating at a 3 or greater on a scale from 0-10 and 1 symptom at any level, 4) life expectancy $\geq$12 months. Exclusion criteria include cognitive impairment (e.g., dementia), 2) presence of a severe psychiatric condition (i.e., psychotic disorder or episode) or a psychiatric condition (e.g., suicidal intent), and 3) inability to converse in English.

*Due to COVID-19, we propose a **temporary** amendment. This temporary amendment requires participants to own their own smartphone to be eligible for participation.

Subject Recruitment and Compensation

- Describe recruitment procedures, including who will introduce the study to potential subjects. Describe how you will ensure that subject selection is equitable and all relevant demographic groups have access to study participation (per 45 CFR 46.111(a) (3)). Include information about approximately how many DUHS subjects will be recruited. If subjects are to be compensated, provide specific prorated amounts to be provided for expenses such as travel and/or lost wages, and/or for inducement to participate.

Subject Recruitment and Compensation. *Focus group and user testing participants will be 40 patients who have undergone HCT and have reported pain, fatigue, and distress post-transplant in addition to 6 healthcare professionals (e.g., nurses, oncologists) who provide care to HCT patients. RCT participants will be 40 patients***.** The amount of time patients are h ospitalized for their HCT varies based on the type of transplant they receive (e.g., autologous vs. allogeneic). Thus, patients who undergo an autologous transplant will be approached either pre- or post-transplant. Pre-transplant approach and consent will happen 1 week to 1 month before a scheduled transplant and post-transplant approach and consent will happen up to 3-months post-transplant. Patients who undergo an allogeneic transplant will be approached within 1-month post-transplant.

Drs. Kelleher (PI) and Somers (Co-I) will work closely with the study oncology physician champion (Dr. Anthony Sung [Co-I]) to facilitate recruitment of patient participants in their clinics. Drs. Kelleher and Somers (Co-I) have worked with the ABMT providers on past trials and successfully recruited cancer patients with pain, fatigue, and distress.

Patient participants will be recruited under a Waiver of Consent and HIPAA authorization. Dr. Sung and his team will provide the study team with the names and medical record number of all participants scheduled for transplant. Then, the study team will gather information from medical records to assess whether or not the patient meets study inclusion criteria (i.e., cancer diagnosis) and is at least 18 years old. The study team will also collect medical information related to transplant type and date to use to appropriately time recruitment. Other information gathered at this time will include cancer type, date of diagnosis, recurrence date, patient date of birth, sex, marital status, education, race, cancer stage, and height/weight. Once a potential study participant has been identified and they are within the study recruitment window, study staff will mail the patient a letter signed by the study PI and oncology physician champion (Anthony Sung, MD) informing them of the study and providing contact information to decline/opt out. We will attempt to meet potential participants at the transplant clinic to attempt recruitment, or by phone if we are unable to meet them in clinic (e.g., due to time constraints). **For patients approached by phone** (e. g., due to time constraints in clinic), we will wait 3 days from mailing the study letter to allow time for the patient to receive the letter. When contacting by phone, the study team member will follow the IRB approved script to introduce and explain the study, describe study procedures, and assess the patient's interest and eligibility. If the patient is interested and eligible, the study team member will schedule a time to meet the patient in clinic or in the study team's research office to obtain written consent (Pain Prevention and Treatment Research Program, 2200 W. Main St., Ste. 340, Durham, NC 27705). **For those approached in clinic**, a member of the medical team known to the patient will first ask the patient’s permission to have a member of the study team approach them. We will not be using cold-contact. Once permission is given, a member of the study team will approach the patient and describe the study procedures. If the patient remains interested, they will

complete the written consent process prior to their participation in the study. A member of the study team will answer any questions that the potential participant may have. Once informed consent has been received, participants will be scheduled for a study appointment either to happen at that time or a time convenient for them in the future. A member of the study team will conduct the appointment. If a participant declines study participation at any point during these procedures, the information provided to the study team through the medical team or medical records will be immediately de-identified. At this first study appointment, the study team member will explain all study procedures and administer the baseline assessment.

Compensation. User testing and RCT participants will receive $20 for completing each of the two study assessments (pre-treatment and post-treatment; total $40). All participants will continue to receive standard medical care from their medical team. No participant will be asked to change or decline any strategies for symptom management based on their participation in this study.

*Due to COVID-19, we propose a **temporary** amendment. This temporary amendment suspends in-clinic approaches. Study staff will continue to mail out a letter, no cold-contact, and then will approach by telephone. Compensation procedures will remain the same.

Consent Process

- Complete the consent section in the iRIS Submission Form.

Subject's Capacity to Give Legally Effective Consent

- If subjects who do not have the capacity to give legally effective consent are included, describe how diminished capacity will be assessed. Will a periodic reassessment occur? If so, when? Will the subject be consented if the decisional capacity improves?

Not applicable.

Study Interventions

- If not already presented in #4 above, describe study-related treatment or use of an investigational drug or biologic (with dosages), or device, or use of another form of intervention (i.e., either physical procedures or manipulation of the subject or the subject's environment) for research purposes.

Study interventions presented in #4 above.

Risk/Benefit Assessment

- Include a thorough description of how risks and discomforts will be minimized (per 45 CFR 46.111(a) (1 and 2)). Consider physical, psychological, legal, economic and social risks as applicable. If vulnerable populations are to be included (such as children, pregnant women, prisoners or cognitively impaired adults), what special precautions will be used to minimize risks to these subjects? Also identify what available alternatives the person has if he/she chooses not to participate in the study. Describe the possible benefits to the subject. What is the importance of the knowledge expected to result from the research?

Risk/Benefit Assessment

*Potential Risks***.** The primary risks of this study are those associated with confidentiality. There is some risk attendant to confidentiality of self-report data. Two password-protected databases will be used for this study to ensure confidentiality. First, a tracking database will be used for recruitment and follow-up. This data will house information related to tracking the participants in the study, such as phone numbers and addresses. No medically sensitive or outcome data will be stored in this database. This database will also track non-participants (i.e., those who have declined participation) only to the barest minimum to ensure that they are not contacted again about participation. At the end of the study, all identifiable data of non-participants such as their names will be deleted. Tracking data on participants will be retained for the usual required period. Second, all study data will be stored in a separate password protected REDCap database without any personal identifiers. Data in this database will be derived from patients' direct input into REDCap, which is an online survey system; data entered into this system is stored on a secure server housed behind the Duke Universtiy Medical Center (DUMC) firewall. Only a unique study identification number will link the electronic data to the study data file. The tracking data and study data will be stored in a file on a secure DUMC psychiatry server which can only be accessed by necessary members of the research team. Access to the Duke network requires a password protected, 128-bit encrypted virtual private network connection provided by Cisco systems.

There are few risks linked to participating in in-clinic activity coaching sessions with an occupational therapist that center on daily steps. The activity coaching component of the intervention is being designed in part by hematology oncology providers and an occupational therapist who specializes in working with hematology oncology patients. Further, the activity coaching sessions will be led by a senior level occupational therapist at Duke University Hospital who holds a lymphedema therapist certification and specializes in working with hematopoietic stem cell transplant (HCT) patients pre- and post-transplant. The activity coaching component of the intervention is consistent with clinical recommendations for activity post-transplant and will be modified based on the patient participant's level of functioning. We will obtain physician clearance for activity prior to initiating the intervention sessions. While we do not anticipate any adverse events, we have developed a protocol to protect against and track adverse events related to exercise injuries /falls, lymphedema flares, hypotension or hypoglycemia, and cardiovascular events.

The risks associated with this study are minimal and rare. During the assessments, participants will be asked to complete a walking test. The 6 minute walk test will be conducted in a hallway at the Duke ABMT Clinic or in a hallway in our research lab office space at the Pain Prevention and Treatment Research Program located in Erwin Square (2200 W. Main St., Ste. 340). Study staff (e.g., CRC, Occupational Therapist) will complete the 6 minute walk test. The 6 minute walk test is optional for participants; if a patient declines, we will not conduct the test. Further, we will check patients' blood pressure prior to conducting the 6 minute walk test and if any of the following contraindications are present, we will not conduct the test: (1) unstable angina during the previous month, (2) myocardial infarction during the previous month, (3) resting heart rate >120, (4) systolic blood pressure >180 mm Hg, (5) Diastolic blood pressure >100 mm Hg. There are some risks associated with the 6 minute walk test. During the 6 minute walk test, a participant may experience difficulty with breathing, shortness of breath, chest pains, dizziness, and/or light headedness. There is also the potential risk of a fall during the 6 minute walk. The study investigators, including the medical oncologist co-investigator, and the study team will take all precautions possible to avoid and minimize these risks (e.g., checking blood pressure and other contraindications prior to conducting test, making test optional). Should any of these occur, appropriate emergency care (e.g., 911) will be provided. A defibrillator is

available at the ABMT Clinic, and so are nursing and other medically trained staff. Over the course of the intervention, participants will be asked to participate in in-person/in-clinic activity coaching sessions led by a certified, senior level occupational therapist and to continue this activity and skills practice on their own at home. While we do not anticipate any adverse events and the intervention is consistent with physical activity recommendations, participants may be at risk for adverse events related to physical activity such as injuries/falls, lymphedema flares, hypotension or hypoglycemia, and cardiovascular events. Again, we will obtain physician clearance for activity prior to initiating the intervention sessions and should any of these adverse events occur, appropriate emergency care (e.g., 911) will be provided. Overall, the benefits of the intervention outweigh the risks and the activity coaching component is consistent with recommendations from HCT oncology providers, occupational therapists specializing in HCT care, and national guidelines for HCT patients.

Potential Benefits and Importance of Information to be Gained. This study has several potential benefits. First, hematopoietic stem cell transplant patients with pain, fatigue, and psychological distress who participate in the intervention may learn ways to enhance their symptom coping strategies and increase their physical activity. Intervention participants may experience significant decreases in symptom severity and physical disability as well as increases in physical and psychological functioning. Second, if the proposed HCT Symptoms and Steps protocol proves to be feasible, acceptable, and shows promise for efficacy, it could be applicable to a number of patient populations with a similarly high symptom burden who face challenges similar to hematopoietic stem cell transplant patients with pain, fatigue, and distress. Third, the proposed model of intervention delivery has the potential to be expanded to intervene on a number of other needs faced by patients with chronic illness (e.g., medication adherence, caregiver burden). The proposed intervention model has the potential to dramatically redesign existing modes of behavioral intervention delivery, improve continuity and coordination of care, and improve patient outcomes.

Costs to the Subject

- Describe and justify any costs that the subject will incur as a result of participation; ordinarily, subjects should not be expected to pay for research without receiving direct benefit.

There are no costs to the subject other than the time that is required to participate in the study.

Data Analysis & Statistical Considerations

- Describe endpoints and power calculations. Provide a detailed description of how study data will be analyzed, including statistical methods used, and how ineligible subjects will be handled and which subjects will be included for analysis. Include planned sample size justification. Provide estimated time to target accrual and accrual rate. Describe interim analysis including plans to stop accrual during monitoring. Phase I studies, include dose escalation schema and criteria for dose escalation with definition of MTD and DLT.

Data Analysis & Statistical Considerations

Sample Size. Study goals are intervention protocol and mobile app development, feasibility, acceptability, and initial outcome patterns suggesting efficacy of a psychosocial intervention. We have used sample sizes from 15-40 to test feasibility, acceptability, and outcome patterns suggesting efficacy of a novel intervention or intervention delivery, successfully publishing these trials[59,60] and using data to secure larger funding.

Aim 1 Analyses. Focus groups will be audio-recorded and transcribed. Recordings and transcripts will be reviewed by Drs. Kelleher and Somers. These reviews will refine the discussion guide for the subsequent focus group. Data analyses will be based on a grounded theory approach,[61] which has been used by Dr. Somers in development of other psychosocial interventions for patients with cancer.

Aim 2 Analyses. Feasibility will be assessed by examining accrual, adherence, and attrition. *Accrual* will be indicated by meeting the recruitment goal of 40 participants in 12 months. Descriptive statistics will be used to report the number of HCT patients screened and determine rates of non-eligibility and refusal. *Adherence* will be indicated by calculating the proportion successfully completing all intervention sessions within the HCT Symptoms and Steps arm and the proportion completing post-treatment assessments within each arm. 80% completed intervention sessions and 80% completed assessments will serve as our feasibility benchmark. If less than 40% of participants complete all intervention sessions and assessments, HCT Symptoms and Steps will not be considered feasible. *Attrition* will be indicated by 80% of consented participants completing the study protocol (i.e., remain enrolled). **Acceptability** will be indicated by 80% of patients reporting satisfaction with HCT Symptoms and Steps (M=7) on the CSQ.

Aim 3 Analyses. Between-group effect sizes will be used to evaluate treatment effects on physical disability, as well as pain, fatigue, psychological distress, physical activity, and self-efficacy for symptom management. Between-group effect sizes will provide an index of relative change for HCT Symptoms and Steps participants vs. HCT Education participants. Because small samples can differ on pretest scores, effect sizes will be calculated by first creating change scores for each person. The between-group effect size will then be calculated by subtracting the average HCT Education group change score from the average HCT Symptoms and Steps change score, and dividing this difference by the standard deviation of the pooled treatment/control group's change score. This study is not designed to make conclusions about efficacy without further study.

Data & Safety Monitoring

- Summarize safety concerns, and describe the methods to monitor research subjects and their data to ensure their safety, including who will monitor the data, and the frequency of such monitoring. If a data monitoring committee will be used, describe its operation, including stopping rules and frequency of review, and if it is independent of the sponsor (per 45 CFR 46.111(a) (6)).

Data & Safety Monitoring

This trial carries minimal risk. There are not physical or side effects involved in taking part in this study. The protocol does not use an investigational drug, procedure, or device. Regardless, all adverse events, serious and non-serious, will be fully documented in the appropriate adverse event form approved by the Duke University Medical Center IRB. For each event, the investigator will provide the onset, duration, intensity, treatment required, outcome, and action taken. Any serious or significant study-related adverse event, whether or not the investigational protocol has been administered, will be reported promptly to the IRB. All patients in the study will continue their usual care during the course of the study, thus their doctors will provide monitoring of the patients' overall medical status. All research personnel who have direct contact with patients will be trained to observe and report any

adverse events to the principal investigator. The principal investigator will report any adverse events to the institutional review board at Duke University and to the NIH. An adverse event is defined as any untoward medical occurrence during the clinical investigation that has a causal relationship to the study protocol. A serious adverse event is defined as any event which results in death, is immediately life threatening, results in persistent or significant disability/incapacity, patient hospitalization, or is serious for any other reason representing significant hazard. All adverse events will be reported to Duke's IRB in real time. All data will be stored on a secure server with multiple backups created regularly. The data manager, Maggie Rogers, and the co-investigator, Tamara Somers, PhD, will monitor the data on a monthly basis.

All interactions with study participants will be under the direction of a Licensed Clinical Psychologist (Drs. Kelleher [PI] and Somers [Co-I]). Interventionists in this trial will have experience with distressed patients with chronic disease. They will be trained, specifically in the context of this trial, to monitor for any signs that participants are experiencing high levels of physical or emotional distress that need to be addressed outside the context of this trial. If this is determined to be the case, the PI will work directly with the participant to move forward in a way that is in the best interest of the patient. No participant will be kept in the trial if they are experiencing increased or extreme distress. Interventionists in this trial will be carefully trained to monitor participants' psychologist status and report to the PI. Dr. Kelleher (PI) will be contacted when emotional distress is identified in a participant. Dr. Kelleher works directly with the Cancer Patient Support Program at Duke Cancer Institute as a practicing licensed clinical psychologist and as a supervisor to psychology trainees (i. e., advanced graduate students, clinical psychology interns); she is integrated into the psychosocial care program at the cancer center and has experience referring cancer patients who are distressed to appropriate psychosocial or psychiatric care within this large team of mental health professionals. She will use the same resources when making referrals for distress participants in this study.

Privacy, Data Storage & Confidentiality

- Complete the Privacy and Confidentiality section of the iRIS submission form.

Describe Role of External Personnel:

Not applicable.