DF/HCC NON-CLINICAL PROTOCOL

PROTOCOL TITLE:

Development of a positive psychology intervention to improve mood and health related quality of life in patients post hematopoietic stem cell transplantation- Proof of Concept Trial

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1.0 Objectives*

1.1 Purpose

The purpose of this study is to perform a proof-of-concept trial for a novel phone-based positive psychology intervention for hematopoietic stem cell transplant (HSCT) patients to assess feasibility and acceptability of the intervention prior to a larger pilot study.

1.2 Specific Aims/Objectives

Specific Aim #1 (Feasibility and Acceptability; primary aim): To assess whether the novel positive psychology intervention is feasible (participants will complete 5 out of 8 phone sessions) and acceptable in HSCT patients.

Specific Aim #2 (Effects on psychological outcomes): To assess whether this preliminary intervention appears to result in improvement in positive affect and other psychological well-being factors as measured by dispositional optimism, anxiety, and depression.

Specific Aim #3 (Effects on other outcomes): To examine the impact of the intervention on overall function and health-related quality of life.

1.3 Hypothesis

Hypothesis #1: The PP exercises will be feasible (i.e., 5 of the 8 phone sessions will be completed by a majority of patients) and acceptable (mean score of at least 6 out of 10 on ratings of ease of completion and subjective utility of the exercises). Furthermore, we will obtain complete objective follow-up data in at least 80% of enrolled participants at the end of the intervention.

Hypothesis #2: The intervention will lead to improvements in positive affect and other psychological well-being factors as measured by dispositional optimism, anxiety, and depression at completion compared to baseline.

Hypothesis #3: The intervention will lead to improvements in health-related quality of life and functional outcomes at completion compared to baseline.

2.0 Background*

2.1 Scientific or scholarly background and Significance.

Hematopoietic stem cell transplantation (HSCT) is the transplantation of stem cells (either from the patient themselves [autologous], or a donor [allogeneic]) derived from bone marrow or from peripheral or cord blood for the treatment of blood or bone marrow

malignancies including leukemias, lymphomas, mylodysplastic syndromes and myelomas. About 22,000 HSCTs take place annually in the United States.

Adherence to frequent clinic visits, active medication management and health behaviors such as healthy diet and regular physical activity is essential for a successful routine follow-up care after HSCT. Additionally, HSCT patients and their caregivers are required to constantly monitor for risks and symptoms of infections, graft vs. host disease, or relapse, and such vigilance requires high psychological well-being and motivation.[2]

Most HSCT patients are not clinically depressed. However, many experience deficits in psychological well-being (e.g., optimism or positive affect). Low levels of positive states and constructs contribute to fatigue and reduced physical functioning, which inevitably can negatively impact the successful adherence to the intensive follow-up care required after HSCT, health-related quality of life and overall long-term recovery. Importantly, positive states and depression are not simply mirror images of each other (and are only modestly inversely correlated), and the beneficial effects of positive states on outcomes in medical illnesses persist even after accounting for depression/negative affect. This suggests that it is not simply an absence of depression that confers the benefit associated with positive emotions. Indeed, in a wide variety of chronic medical conditions, positive psychological interventions (including exercises to cultivate gratitude, acts of kindness, recall positive life events, and express optimism) completed in a systematic deliberate manner have been prospectively linked to improved well-being, reduced distress/depression, improved medication adherence, and more physical activity.

Although PP states have been shown to positively impact the adherence to health behaviors in patients with chronic medical illnesses, it has not been studied in HSCT patients. Also, there is minimal understanding and report of the deficits in positive emotional states (e.g., optimism or positive affect) in HSCT patients. Additionally, interventions that help boost PP states in HSCT patients have been minimally studied despite their well-documented overall efficacy in other medical populations. We have completed a systematic review of the literature on PP constructs and interventions in HSCT; our review did not yield any preexisting studies that have used PP interventions in any HSCT population.

A PP intervention, consisting of simple, enjoyable exercises that can be delivered via phone by clinicians with a wide range of training, may provide substantial benefit. PP states have been prospectively linked with superior long-term health outcomes and survival in medically ill persons, independent of medical or socio-demographic variables. Additionally, the prospective association between positive states and mortality demonstrated in patients with chronic medical conditions is usually independent of negative emotional states and relevant medical factors. Although PP interventions are easy to deliver and could boost mood and health-related quality of life (HRQoL) in many HSCT patients, they have never been tested in this population.

2.2 Prior Experience and gaps in current knowledge.

Prior to this work with HSCT patients, Dr. Lokko has been the site principal investigator for observational and intervention studies as well as randomized control

trials focusing on positive psychological states and PP interventions in acute coronary syndrome patients to improve cardiac health behaviors.

Dr. Lokko has also just completed qualitative research (Protocol # 17-154) in HSCT patients at the DFCI to learn more about the psychological experiences (both positive and negative) of patients who have hematologic malignancies who have received HSCT. Dr. Lokko successfully enrolled 25 patients for 30-60 minute interviews at two time points. Hence she has experience recruiting this patient population, administering validated questionnaires and instruments in addition to working with these patients clinically on the inpatient psychiatry consult service. Dr. Lokko attends the weekly HSCT team meetings, interfaces with the various clinicians who care for this patient population and has gained familiarity with the patient population, their hospital course after transplant and some of the challenges associated with the immediate recovery phase.

Dr. Lokko is currently working on a systematic review on the association of positive psychological constructs on various psychological and medical outcomes in HSCT- to her knowledge there are no current systematic reviews looking at the association between positive psychological constructs in HSCT.

As mentioned in an earlier section, although PP interventions have been shown to positively impact different psychological and functional outcomes in other chronic medical populations, it has not been studied in HSCT. We hope to address this gap in knowledge by testing the feasibility and impact of a novel PP-based intervention that has been adapted for HSCT patients. It is our hope that this PP intervention will provide a breadth of significant health benefits for HSCT patients and their well-being.

2.3 Relevant Preliminary Studies.

In the first phase of the treatment development (Protocol # 17-154), we aimed to explore and understand the deficits in positive psychological states in this population to inform the creation of our novel PP intervention for HSCT patients. We have successfully performed qualitative interviews (N=25) in approximately the first 30 to 100 days post HSCT to learn about: a) the emotional states (both positive and negative), health behaviors, quality of life and function, b) the sources of emotional states, c) potential links between positive emotional deficits and quality of life and function and d) the utility of potential PP exercise in HSCT patients.

Some of the lessons from the preliminary analysis of the first phase of the study are outlined as follows: 1) Patients embraced the opportunities to share about their experiences with HSCT; 2) Patients experience both positive and negative emotions as part of the HSCT recovery and these emotions impact patient's overall function and quality of life; 3) Patients are interested in increasing positive emotions during HSCT recovery; and 4) The burden of side effects and complications in the first 60 days post HSCT varies significantly among patients and may be challenging for patients to actively participate in an intervention. With the information from our qualitative research phase

and existing literature, we have developed a customized, PP health intervention for HSCT patients.

In the current phase of the treatment development (Phase 2: Refining the intervention), we will perform a proof-of-concept trail (N=25) to ensure our intervention's initial feasibility and to refine the intervention for a larger pilot study.

Essentially, for this phase of the project we hope to do the following:

1. Test an 8-week, telephone-delivered PP intervention in a brief, non-randomized, proof-of-concept trial (N=25).
2. Determine whether this initial intervention is feasible and acceptable in this cohort of HSCT patients.
3. Explore potential benefits of the intervention on outcomes of interest (e.g., optimism, positive affect).

3.0 Inclusion and Exclusion Criteria*

Study participants will be adult (age ≥18) English speaking patients with hematologic malignancies recruited from the Dana Farber Cancer Institute (DFCI) HSCT Program who have access to a phone. Eligible study participants will be identified during the weekly HSCT program meeting, where all transplant attending physicians, physician assistants, nurse practitioners, and infectious disease clinicians review all the upcoming scheduled admissions and discharges as well as the hospital course of admitted patients. Patients who have been approved for the study by their transplant attending physicians at the DFCI weekly transplant meeting who are clinically stable during their HSCT hospitalization will be approached by principal investigator. Willing patients will be told the details of the study and inclusion/exclusion criteria will be assessed. Eligible study participants will then be consented and screened for the study.

The DFCI will register eligible participants in the Clinical Trials Management System (CTMS) OnCore as required by DF/HCC SOP REGIST-101. When required by REGIST-101, registration must occur prior to the initiation of protocol-specific procedures or assessments.

<u>Inclusion Criteria:</u>

- Adult patients with hematologic malignancies hospitalized for allogeneic HSCT at the DFCI inpatient units who are medically stable and appropriate for study approach.
- Ability to speak, read and write English
- Access to a telephone

<u>Exclusion Criteria:</u>

- Current major depressive episode, bipolar disorder, psychosis or active substance use disorder diagnosed via the Mini International Neuropsychiatric Interview (MINI) given that they require more intensive

psychological and psychiatric care. We will however enroll patients with moderate mood and anxiety symptoms as they are likely to benefit from a PP intervention and incorporating their experiences will be useful.

- Cognitive deficits impeding a study participant's ability to provide informed consent or participate adequately in the study assessed via a commonly used 6-item cognitive assessment with the Brief Interview for Mental Status (BIMS) screening tool that is sensitive and specific for screening for cognitive impairment in research subjects.
- Medical conditions precluding interviews.

Special Populations

- Individuals who are unable to consent or are not yet adults (including infants, children, teenagers), pregnant women or prisoners will be excluded from the study

4.0 Study-Wide Number of Subjects*

We are recruiting 25 patients from only one site. This is not a multisite study.

5.0 Study-Wide Recruitment Methods

This is not a multicenter study and all subjects will be recruited from one local site.

6.0 Multi-Site Research

This study is located to one study site which is the DFCI main campus in Longwood.

7.0 Study Timelines*

7.1 Subject Participation in the study

The planned duration of total participant participation in the intervention is 24 weeks, broken down as follows: at weeks four, eight and twelve following consent and eligibility determination, participants will receive check-in/psychosocial support phone calls about their recovery, then week 14 is for self-assessment questionnaires prior to the 8-session weekly positive psychology treatment, and the last week will be used for a repeat of self-report measures obtained at baseline. Patients will also be given the option to complete self-reported measures via mail vs. phone.

Based on prior recent experience with recruitment from this patient population, we anticipate about 6-months for the total number of patients for the study.

We are estimating the study will be completed in June 2019.

	Enrollment	Check-In/Psychosocial support phone calls (weeks, 4, 8, 12)	Pre-Intervention Visit	Week 1 of PP-intervention	Week 2 of PP-intervention	Week 3 of PP-intervention	Week 4 of PP-intervention	Week 5 of PP-intervention	Week 6 of PP-intervention	Week 7 of PP-intervention	Week 8 of PP-intervention	Follow-Up Session
HSCT team meeting review to confirm eligibility	X											
Assessment of inclusion criteria	X											
Obtain Consent	X											
10-min phone call		X										
PP exercise				X	X	X	X	X	X	X	X	
Follow-up session												X
Self-report measures (LOT-R, PANAS, HADS, PROMIS-PF-20, **PROMIS-Fatigue-8a,** FACT-BMT)	X		X									X

8.0 Study Endpoints*

Primary Endpoint: Establishing the positive psychology intervention feasibility and acceptability in HSCT patients will be the primary endpoint.

Secondary Endpoint: Assessing the immediate impact of the PP intervention on participants' positive psychological state and psychological well-being (as measured by dispositional optimism, positive affect, anxiety and depression, adherence and functional outcomes) will be the secondary endpoint.

There are currently no anticipated primary or secondary safety endpoints.

9.0 Procedures Involved*

9.1 Study Design

The goals of this study are to assess the feasibility, acceptability and preliminary impact of this novel 8-session weekly PP-based intervention for HSCT patients.

Patients will be approached close to their discharge from the hospital after their HSCT for eligibility determination and to obtain consent. After consent is obtained, eligibility will be determined with the mini international neuropsychiatric interview (MINI) and a brief cognitive assessment (with the BIMS) to exclude patients who need more intensive psychological or psychiatric care or have cognitive deficits. Upon agreement and consent to participate in the study, participants will receive check-in/psychosocial support phone calls at weeks four, eight and twelve to provide support and check-in on how their recovery is going since discharge, develop rapport and prepare them for the positive psychology treatment portion of the intervention which will start between Day 90-120 post HSCT. Between the 90-120-day point, when patients return to the clinic for their routine 100-day post HSCT follow-up, the interventionist/principal investigator will meet briefly with the patients in clinic to complete self-assessment questionnaires to measure positive affect, optimism, anxiety, depression, HSCT-specific health related quality of life, adherence and overall function. For the rare situations when participants cannot complete these self-assessment questionnaires in person, patients will be given the option to complete self-assessment questionnaires by phone or mail.

After completion of the questionnaires, participants will be provided with a treatment manual, with weekly PP exercises for 8-sessions. All participants will be asked to complete 8 weekly PP exercises and will be asked to speak with the study interventionist, in this case the principal investigator, weekly. Immediately after the completion of the exercises, the participants will rate the ease of exercise completion, overall utility of the exercise, and their current levels of positive affect. For the last week of the intervention, baseline self-assessment questionnaires will be reviewed. At study completion, we will inquire about participants' potential interest in being contacted about our future studies. We will adhere to any and all participant requests regarding contact.

9.2 *Research Procedures*

Psychosocial Support/Check-In phone calls: Study participants will receive monthly phone calls from the study interventionist/principal investigator at weeks four, eight and twelve following their enrollment. The goal of the psychosocial support/check-in phone calls is to provide study participants an avenue to talk about their adjustment and transition to the outpatient care from inpatient, quality of life and coping during recovery, adherence to treatment, etc…which will be beneficial to patients

and help with rapport building with the interventionist prior to the positive psychology intervention.

Pre-intervention visit: The first physical contact with the patient since consent and enrollment during the HSCT hospitalization will be at the routine 100-day follow-up visit (around Day 90-120) in clinic. The visit will happen in a private room at in the DFCI outpatient clinic. Patients will complete the following self-assessment scales: Positive and Negative Affective Scale (PANAS) to measure positive affect, Life Orientation Test-Revised [LOT-R] to measure optimism and the Hospital Anxiety and Depression Scale [HADS] to measure anxiety and depression. We will also assess HSCT-specific HRQoL with the Functional Assessment of Cancer Therapy-Bone Marrow Transplantation [FACT-BMT] scale), overall function (PROMIS-PF-20), and fatigue (PROMIS-Fatigue-8a). Data about medical and oncologic history, treatment course and medications will be obtained from the electronic medical record. – A waiver of HIPAA authorization would be requested for this and will only be clarified with patients if there are inconsistencies in the medical records. This in person session should take about 30 minutes. Patients will also be given the option to complete this visit over phone if in person visit cannot be coordinated with other routine 100-day follow-up care.

After completion of the questionnaires, participants will be provided with a treatment manual, with weekly PP exercises. Participants will be assigned the first exercise (gratitude for positive events) in preparation for their first phone session.

Weekly phone sessions for positive psychology intervention: All participants will be asked to complete 8 weekly PP exercises and to speak with the interventionist weekly. Weekly phone sessions will last approximately 30 minutes. Prior to completing each phone session, participants will be asked to rate their current level of happiness and optimism, using a 10-point Likert scale. Immediately after completing the exercise and phone session, participants will rate the ease of exercise/session completion, overall utility of the exercise/phone session, and their current levels of happiness and optimism, all using 10-point Likert scales. These calls will be recorded so that a percentage (10%) of these recordings can be reviewed by research mentor, Dr. Huffman to ensure that the PP intervention is being delivered as described in the protocol.

Follow-up session: The last week of the study will be used for a repeat of the self-assessment questionnaires obtained at the beginning of the study. This will be done either via phone or mail depending on patient preference.

Positive Psychology Program Content. All phone sessions will include (a) a review of the ease and utility of the week's PP exercise (b) a discussion of the

rationale of the next week's PP exercise through a guided review of the PP manual, and (c) assignment of the next week's PP exercise. During the calls, the interventionist and participant will also review the next section of the treatment manual and prepare for the upcoming week's exercise.

Positive Psychology Exercises. The PP exercises used in this study were selected based on the qualitative study results from the first phase of this study (IRB: 17-154), their superior performance in our pre-pilot research and others' work with medical populations. They will be grouped into three modules focusing on a different psychological state:

Module 1: Gratitude-based activities

Week 1: Gratitude for positive events.
Participants recall three events, small or large, in the preceding week that were associated with satisfaction, happiness, pride, or other positive states.

Week 2: Expressing gratitude.
Participants write a letter of gratitude thanking a person for an act of kindness; participants may, at their discretion, share the letter with the other person.

Module 2: Strength-based activities

Week 3: Remembering a past success.
Participants recall a prior event in which they experienced success. They write about the event, their contribution to the success, and the positive feelings evoked by recalling it. Finally, they consider how they might use the experience to be successful in the future.

Week 4: Using personal strengths.
Participants choose a personal strength that is important to them and then find a new way to use that strength over the following week.

Week 5: Using Perseverance
Participants work to learn the skills of sticking with something when things get though especially as it pertains to their recovery from the transplant.

Module 3: Meaning-based activities

Week 6: Enjoyable and meaningful activities.
Participants complete a series of self-selected activities that vary between those that bring immediate boosts in mood and those that are more deeply meaningful.

Week 7: The Good Life
Participants work to articulate what their values are and what their perception of a good life will look like especially as it pertains to their health and recovery.

Week 8: Planning for the Future.
Participants work to perform enjoyable and meaningful acts for themselves and others in daily life. Trainers help participants create a plan for using these skills on their own in the near future.

Follow-Up Session
At the last week of the study, a member of the study staff will call participants to repeat the self-report questionnaires that were administered at baseline. Positive and Negative Affective Scale (PANAS) to measure positive affect, Life Orientation Test-Revised [LOT-R] to measure optimism and the Hospital Anxiety and Depression Scale [HADS] to measure anxiety and depression. We will also assess HSCT-specific HRQoL with the Functional Assessment of Cancer Therapy-Bone Marrow Transplantation [FACT-BMT] scale), fatigue (PROMIS-Fatigue-8a) and overall function (PROMIS-PF-20). Finally, patients will be asked about their experience in the study, including any aspects of the intervention or study procedures that could be improved. In sum, these scales should take approximately 30-40 minutes to complete. If participants would rather complete the follow-up questionnaires in written form rather than over the phone, we will send them a paper packet at the time of the follow-up.

Given the results of our prior PP studies in medical populations yielding a 64-85% completion rate of the exercises, and given that this is a feasibility study (i.e., we want to assess participants' willingness to complete the phone sessions), we will expect participants to complete at least 5 PP exercises. In other words, if a participant completes at least 5 sessions, missed sessions will not be considered a deviation from the protocol.

Training. The PP exercises for this trial have been identified via published literature, or directly from researchers, and modified appropriately for this population based on results from first phase of the study that the IRB approved (17-154). Additional text outlining the rationale and instructions for each exercise are in the written packets for each exercise that are provided to participants. Dr. Lokko will engage in several training exercises prior to study initiation. Dr. Lokko's research mentor, Dr. Jeff Huffman, and his research group have had substantial experience in explaining and delivering PP exercises from their studies in cardiac and psychiatric patients, which will inform Dr. Lokko's training. Together with Dr. Huffman, Dr. Lokko will review the treatment manual and the team's prior training manuals related to these exercises. They then will complete all exercises together to gain experience performing and reviewing each exercise.

9.3 Procedures performed to lessen the probability or magnitude of risks.

Confidentiality. As with any study, there is the risk of a breach of confidentiality; these risks will be minimized by using participant identification numbers rather than

identifying personal data on study documents, and by using locked cabinets/offices and password-protected databases to store personal information. Only study staff (the PI, the research assistant entering data) will have any access to personally identifiable information about participants, and such access will be limited only to information necessary to complete study tasks. We will ensure that contact with participants is confidential by using only the phone numbers and other contact information that are specifically allowed by the participants and not leaving study-related messages for participants unless expressly allowed by participants. Upon enrollment, we ask all participants if it is acceptable to leave voice messages on their phones, as well as the appropriate times to call them. We adhere to any and all patient requests regarding contact.

Digital recordings of the sessions will be completed using portable recorders. If a study participant were to refuse audio recordings, they can either remove themselves from the study or work with the study investigator to choose an alternative to audio recording such as transcription. The principal investigator and the senior research mentor will randomly-select recorded phone sessions to review for competence and adherence to the protocol. All recordings will be downloaded immediately from the recorders and the electronic files will be kept within the firewalled, password-protected file on a Partners server. Recordings will contain no personally identifiable information (and principal investigator will not use names or other identifying information on the recordings) and will be erased following review.

Informed consent process. Regarding the consent process, we will approach/recruit participants in the hospital only after their clinicians in the HSCT transplant team have approved for them to be approached. When discussing the study, we will emphasize the study's optional nature and participants' ability to opt out/un-enroll at any time, for any reason.

Medical & psychiatric emergencies. If patients report acute medical symptoms, they will be directed to emergency medical care, and their primary medical physicians may be contacted as needed. If study staff have questions regarding medical symptoms and their urgency, patients' primary oncologist and their HSCT clinicians and the PI will be available to consult (and call patient) as needed. We will ask participants to report adverse events related to study participation they may have experienced at any time throughout the study.

We will obtain data using different measures as listed below. We will also check the patient electronic medical records to confirm baseline demographic information. The measures we will use are as follows:

- Optimism: LOT-R
- Positive affect: Positive Items on the PANAS
- Anxiety/depression: HADS
- HSCT-related QoL: FACT-BMT

- Overall function: PROMIS-PF-20
- Fatigue: PROMIS-Fatigue-8a

9.4 Long-term follow-up.

This study does not have long-term follow-up as part of the protocol. As aforementioned, the last week of the program entails obtaining some feedback about patient's perception of the intervention, as well as a repeat of the baseline questionnaires.

10.0 Data and Specimen Banking

We will not be collecting any data or specimen that will need banking for this study.

11.0 Data Management* and Confidentiality

11.1 Data analysis plan, including any statistical procedures.

Data will be downloaded from REDCap into the Stata statistical package. For Aims 1 and 2 (feasibility, acceptability, and immediate impact), descriptive statistics will be used to report proportion of phone session completion and mean scores on exercise ratings.

To compare mean scores on outcome variables for Aim 3, paired t tests will be used to explore mean differences between baseline and follow-up values. All statistical tests will be two-tailed and $p<.05$ considered significant, though this study will not be powered to detect statistically significant differences between baseline and follow-up points. Given the sample size and potential for drop-out, we will also consider alternatives to a t-test such as non-parametric tests, effect size calculations to support feasibility of study assessment procedures.

11.2 Power analysis.

This exploratory proof-of-concept study with 25 patients (anticipated 10 patients to complete the study), as noted, will not be powered to detect statistically significant differences between baseline and follow-up points, and is designed to assess feasibility of methods.

11.3 Data Security Plan.

All source data (e.g., chart review data and participant self-report) will be entered into the REDCap database. The PI (Dr. Lokko) will review this data to ensure that it is being entered correctly and will perform 'test downloads' of the data to ensure that it can be captured in the statistical package to be used in this study. We will also use

locked cabinets/offices and password-protected databases to store personal information. Only study staff (currently just the PI) will have any access to personally identifiable information about participants, and such access will be limited only to information necessary to complete study tasks.

We will ensure that contact with participants is confidential by using only the phone numbers and other contact information that are specifically allowed by the participants and not leaving study-related messages for participants unless expressly allowed by participants. Upon enrollment, we ask all participants if it is acceptable to leave voice messages on their phones, as well as the appropriate times to call them. We adhere to all patient requests regarding contact.

11.4 Quality Control.

Safety monitoring will be performed by Dr. Lokko (PI), who will ensure that the study team is adequately identifying, reviewing, and reporting adverse events and unanticipated problems to the Institutional Review Board (IRB). A more detailed description of monitoring mechanisms, intervals, and the information monitored is outlined below.

Monitoring mechanism: Dr. Lokko (PI) will take primary responsibility for the data safety monitoring. However, this study will have a formal data safety monitoring board (DSMB), which will be chaired by Dr. Jeff Huffman (psychiatry, primary mentor), and populated by Dr. Chris Celano (psychiatry, peer-mentor), and Dr. Rachel Millstein (psychologist, external to study).

Monitoring intervals: Monitoring of adverse events will occur on an ongoing basis with notification of Dr. Lokko with any adverse study-related events. More systematic weekly meetings for review of feasibility/acceptability information and minor IRB deviations will be held between Dr. Lokko and Dr. Huffman. Dr. Lokko will then discuss any potential issues regarding data safety or protocol deviations with Dr. Huffman during weekly supervision meetings. This allows the team to review this information and adjust procedures as required. Furthermore, monthly journal clubs are held with the study team; these include discussions of related projects (e.g., studies of physical activity in cardiac patients, studies of positive psychological interventions). Finally, the formal DSMB will meet every four months to monitor patient safety outcomes. These ongoing, weekly, and intermittent reviews ensure that the study procedures minimize research-related risk by reviewing specific

outcomes linked to the project and by reviewing relevant literature to ensure that interventions are best practice.

Information to be monitored: Information to be monitored will include: (a) an evaluation of the progress of the research study, including assessments of data quality and timeliness and participant recruitment, accrual and retention consistent with plans for diversity and generalizability, (b) a review of study safety data—adverse event (and minor deviation) information—to determine whether the study should continue as originally designed, be changed, or be stopped, (c) review of procedures to maintain participant confidentiality (e.g., storage of identifiable information in locked cabinets, ensuring study databases have no personal identifying information, use of study participant numbers on communications about the study), and (d) an assessment of external factors or relevant information (e.g., developments in the literature, results of related studies, etc.) that may have an impact on the safety of participants or on the ethics of the research study, such as through the journal club listed above.

12.0 Provision to Monitor the Data to Ensure the Safety of Subjects

This research does not require or involve more than minimal risk to subjects.

13.0 Withdrawal of Subjects*

We do not anticipate any circumstances under which the subjects will be withdrawn from the research without their consent. We do not anticipate any termination of patients. When informed consent is being obtained from patients, we will emphasize to patients that they can withdraw from the study at any time for any discomforts. Subjects who withdraw from the study will still have their data potentially analyzed depending on when in the study they withdraw and patients will be informed of this as well. We will ensure that contact with participants is confidential by using only the phone numbers and other contact information that are specifically allowed by the participants and not leaving study-related messages for participants unless expressly allowed by participants. Upon enrollment, we ask all participants if it is acceptable to leave voice messages on their phones, as well as the appropriate times to call them. We adhere to any and all patient requests regarding contact.

14.0 Risks to Subjects*

The risks to participating in this study should be relatively limited. We anticipate no physical risks to participating in this study. Study participants may experience discomfort from discussing psychological experiences and could experience the evaluation as intrusive. Study participants who do not find any benefit from participation may find this upsetting. Activities to obtain data through the follow-up assessment may also provide some inconvenience to study participants. We will take all measures to ensure patient comfort and will postpone or end interviews at study participants' requests. We will also ensure that the PI or other psychiatry study staff is available to intervene if needed (due to patient discomfort or to answer specific questions about the study), during baseline and phone assessments. We have used the briefest methods necessary to assess emotional states and other outcomes to reduce patient discomfort.

As with any study, there is the risk of a breach of confidentiality of data collected. To minimize the potential loss of confidentiality, we will employ multiple safeguards and measures. Interviews will be administered by trained interviewwes. Study participants will be assigned a unique study identification number which will be stored separately from personal identification information. All data, including telephone recordings and transcripts will be securely stored in locked file drawers. All project file cabinets and computer databases will be secured in locked offices. We will ensure to not provide any data to third particies. Data will be aggregated and summary reports will be generated without any personal identification information.

15.0 Potential Benefits to Subjects*

Patients may not benefit from participating in this study. However, as part of the intervention, patients may obtain benefit from sharing their experiences especially as they explore and notice their positive experiences more than baseline. Contact with study interventionist and principal investigator may also provide support and social connection for study participants during the high risk post-discharge period of HSCT recovery. Patients will be given the opportunity to identify positive emotions and consider ways to enhance their own positive emotions. Description of the PP exercises may enlighten them as to potential means of improving their own emotional states. Furthermore, they will have the opportunity to consider possible barriers to adherence to health-related behaviors. Patients who are identified as suffering from depression on the HADS scale will be offered opportunities to get treatment for such symptoms.
Optimism and other positive affective states are prospectively associated with increased participation in healthy behaviors in other medically ill populations and HSCT patients may benefit from this as well. This study therefore has the potential to identify key factors related to overall function, quality of life and adherence to health behaviors in HSCT patients. The creation of a PP-based intervention—based on this qualitative research phase—targeted at improving positive emotional states in HSCT patients could lead to a novel approach to enhancing adherence, overall function and quality of life in this population, which in turn might result in decreased morbidity and mortality in this population. Future studies could investigate the feasibility of implementing this

intervention in a similar population and examine the impact on psychological outcomes. If the PP intervention in these studies prove to be feasible, well-accepted, and associated with improvements in physical activity and other key outcomes, it may well be possible to utilize these easily-delivered and completed exercises as part of a clinical care package for HSCT patients. Thus participation in this study may result in substantial benefit to future patients.

16.0 Vulnerable Populations

This project does not involve vulnerable populations including pregnant women, prisoners, adults who cannot consent, children or patients with cognitive difficulties.

17.0 Community-Based Participatory Research

This research does not involve community-based participatory research

18.0 Sharing of Results with Subjects*

We do not anticipate sharing individual subject results with third parties. We hope to publish the results from the study in peer review journal articles but data will be de-identified. Patients will be made aware of the fact that the results will be published.

19.0 Setting

Study participants will be adult (age ≥18) English speaking patients with hematologic malignancies recruited from the Brigham and Women's Hospital (BWH) and Dana Farber Cancer Institute (DFCI) HSCT Program in Brookline, MA. Eligible study participants will be identified during the weekly HSCT program meeting, which reviews all the upcoming scheduled admissions and discharges. Patients will be approached when clinically stable during their HSCT hospitalization in their private hospital rooms at BWH for eligibility determination and to obtain consent. Upon agreement to participate in the study, contact will be maintained with patients from discharge date to day 90-120 post-HSCT via three phone calls at weeks 4, 8, and 12 to check in with patients, cultivate a relationship, and to remind them of study launch. At the 100-day oncology visit at the DFCI Yawkey Building in Brookline, MA, self-assessment questionnaires will be obtained after consent is reaffirmed. The intervention will be delivered via phone and patients will be called on a private phone they designate.

There will be no involvement from a community advisory board and no research will be conducted outside the DFCI or its affiliates.

20.0 Resources Available

The principal investigator has experience recruiting from this patient population and most recently with the successful recruitment of patients for study (IRB 17-154). The PP exercises for this trial have been identified via published literature, or directly from researchers, and modified appropriately for this population based on results from first phase of the IRB approved (17-154). Dr. Lokko will engage in several training exercises prior to study initiation. Dr. Lokko's research mentor, Dr. Jeff Huffman, and his research group have had substantial experience in explaining and delivering PP exercises from their studies in cardiac and psychiatric patients, which will inform Dr. Lokko's training. Together with Dr. Huffman, Dr. Lokko will review the treatment manual and the team's prior training manuals related to these exercises. They then will complete all exercises together to gain experience performing and reviewing each exercise.

We have decided to recruit 25 patients for this feasibility study based on experience from other studies in medical populations involving positive psychology exercises. In the first phase of the study, we recruited 25 patients, a month earlier than our recruitment timeline, an indication that recruiting 25 patients for the feasibility study is reasonable. The DFCI HSCT sees approximately 550 patients annually for a transplant so we are targeting only 1.8% of the patients that come through the HSCT program.

We will also have research assistants who will help with different aspects of the study including organizing materials for the intervention, managing databases, coding qualitative interviews, performing data analysis and organizing documentation for the study.

I will be devoting 40-50% of my productivity time to this research.

Patients will be seen for consent in their private BWH inpatient rooms. They will be seen for baseline data collection in a private outpatient consulting room at the DFCI. All phone communications will be done using DFCI phones.

If patients report acute medical symptoms, they will be directed to emergency medical care, and their primary medical and transplant oncologists may be contacted as needed. If the patient is at imminent risk to self-harm, the study psychiatrist will take all needed steps to ensure emergent psychiatric evaluation, which may include ensuring evaluation in the nearest emergency room. Participants will be informed of these measures to ensure confidentiality—and the limits of confidentiality, such as arranging for emergent medical or psychiatric care if safety is at imminent risk—as part of the informed consent process. However, given that this is a medical rather than a psychiatric population we anticipate the rate of suicidality in this population will be low.

All study staff for the project will meet weekly to discuss progress of the study and to review any changes in the protocol. Currently, the PI is the only study staff but as research assistants come on board to enter and manage databases such as RedCap, the IRB will be notified, they will be oriented to the details of the study protocol, as well as their individual roles in data collection and management.

21.0 Prior Approvals

This research does not involve any prior approvals for subjects.

22.0 Recruitment Methods

Hospital (BWH) and Dana Farber Cancer Institute (DFCI) HSCT Program in Brookline, MA as was approved for protocol 17-154. Eligible study participants will be identified during the aforementioned weekly HSCT program meeting of HSCT attendings, which reviews all the upcoming scheduled admissions and discharges. Patients will be approached when they are medically stable after HSCT in their private hospital rooms at BWH for eligibility determination and to obtain consent. Upon agreement to participate in the study, contact will be maintained with patients from discharge date to day 90-120 of HSCT via three monthly phone calls to check in and to remind them study initiation. At the routine 100-day oncology visit at the DFCI Yawkey Building in Brookline, MA, self-assessment questionnaires will be obtained. Patients will also be given the option to complete self-assessment questionnaires via phone or mail.

DFCI HSCT program will be the source of the subjects for this study.

Eligible study participants will be identified during the weekly HSCT program meeting, which reviews all the upcoming scheduled admissions and discharges.

Patients will be approached based on approval by the HSCT oncologists at the transplant team meeting. Hence there aren't specific materials or advertisements to recruit patients.

Patients will not receive payments for participating in the study.

23.0 Local Number of Subjects

The plan is to accrue 25 subjects locally. We are expecting to enroll about 25 patients with an anticipated number of completers to be 10.

24.0 Provisions to Protect the Privacy Interests of Subjects

In the consent process, it will be emphasized to the patient that at any time during the research, they are free to say they will not participate in the

study. Their decision to participate in any part of the study will not in any way interfere with their care at the DFCI. We will also emphasize that only study staff will have access to the data.

It will be emphasized throughout the study that participants should not feel obligated to answer any questions that is asked of them that causes uneasiness.

Informed consent will be obtained from patient before any information is accessed in their medical records. Only study staff identified with the study will handle patient data. Participants' information will not be shared with third parties or study members who are not directly part of the study.

25.0 Compensation for Research-Related Injury

We do not anticipate any research-related injury to participants.

26.0 Economic Burden to Subjects

We do not anticipate any costs to the subjects because of participation in the research.

27.0 Consent Process

Informed consent will be obtained for the study. Patients identified at the HSCT weekly meeting based on the inclusion and exclusion criteria will be approached by the principal investigator. After a verbal discussion of the study in detail, patients will be given adequate time to read a written IRB-approved consent form and to ask questions. If they desire, study participants will have at least 24 hours to consider enrollment. To ensure that study participants have the capacity to provide informed consent, we will ask them to describe their understanding of the study's purpose and their role (e.g., that they understand the timing of intervention and its purpose, audiotaping of some of the intervention sessions and the purpose for the audiotaping, confidentiality and its limits, our focused review of medical records, and their ability to end participation in the study at any time for any reason). Patients will also be informed of the lag time between consent and study initiation within which they can change their mind about participating in the study during contact with study staff. Before baselines are obtained from patients for study initiation, consent will be reviewed with patients for a final decision.

The informed consent document will cover study purpose, alternative options, study logistics as well as risks and benefits of study participation. The consent will provide contact numbers for questions regarding the study. The consent document will be signed by the study participant and the investigator to the document that the consent took place. The original consent document will be kept in the study's research file and a copy will be provided to the study participant. We plan to follow SOP: Informed Consent Process (CON-100).

28.0 Process to Document Consent in Writing

We plan to follow SOP: Informed Consent Process (CON-100) and the consent document is part of this application.

Our research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context.

29.0 Drugs or Devices

This study does not involve any drugs or devices.