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Feasibility of a positive psychology intervention (PATH) in allogeneic hematopoietic stem cell transplantation survivors: Randomized pilot trial design and methods

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Abstract

Background: Although patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT) experience low levels of positive psychological well-being (PPWB), interventions that specifically boost PPWB in this population are lacking.

Objective: To describe the methods of a randomized controlled trial (RCT) designed to assess the feasibility, acceptability, and preliminary efficacy of a positive psychology intervention (PATH) tailored to the unique needs of HSCT survivors and aimed to decrease anxiety and depression symptoms and boost quality of life (QOL).

Methods: We will conduct a single-institution RCT of a novel nine-week phone-delivered manualized positive psychology intervention compared to usual transplant care in 70 HSCT

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survivors. Allogeneic HSCT survivors at 100 days post-HSCT are eligible for the study. The PATH intervention, tailored to the needs of HSCT survivors in the acute recovery phase, focuses on gratitude, strengths, and meaning. Our primary aims are to determine feasibility (e.g., session completion, rate of recruitment) and acceptability (e.g., weekly session ratings). Our secondary aim is to test the preliminary efficacy of the intervention on patient-reported outcomes (e.g., anxiety symptoms, QOL).

Discussion: If the PATH intervention is feasible, a larger randomized, controlled efficacy trial will be indicated. Additionally, we anticipate that the results from this RCT will guide the development of other clinical trials and larger efficacy studies of positive psychology interventions in vulnerable oncological populations beyond HSCT.

Keywords

Positive psychology; Hematologic malignancies; Hematopoietic stem cell transplantation; Randomized controlled trial; Psycho-oncology

1. Introduction

Although allogeneic hematopoietic stem cell transplantation (HSCT) provides a potential cure for patients with various blood disorders, the treatment is demanding and entails a prolonged recovery [1]. Allogeneic HSCT entails the infusion of stem cells from a donor into a patient with matching human leukocyte antigen types [2]. Patients receiving an allogeneic HSCT spend about four or more weeks in the hospital for the transplant and subsequent recovery period [2,3]. The transplant hospitalization usually commences with conditioning characterized by high-dose chemotherapy and sometimes total body radiation [3]. Allogeneic HSCT recipients can receive potential immune-related benefits but also immune-related side effects from the transplant, such as graft-versus-host disease (GVHD), which entails damage of host organs by the donor graft cells [2]. The intensity of chemotherapy and GVHD symptoms can result in numerous acute and chronic toxic side effects, including infections, bleeding, nausea, vomiting, diarrhea, fatigue, rashes, and sometimes fatal complications [2,3].

In addition to the physical demands of HSCT, patients experience high levels of distress, with 40% reporting clinically significant depression and anxiety symptoms during the HSCT hospitalization [4,5]. Further, in the six months following the HSCT hospitalization, 43% of patients report symptoms of depression and anxiety, and 25% report posttraumatic stress symptoms [4,5]. Consequently, HSCT recipients experience reduced psychological well-being, undermining their quality of life (QOL) and ability to thrive during the treatment and recovery following transplantation [6]. Most supportive interventions intended to promote psychological well-being for patients undergoing HSCT target symptoms of distress during the acute HSCT hospitalization and the immediate recovery period [7–10]. However, there are limited supportive resources tailored to the specific needs of HSCT survivors beyond the immediate recovery phase after HSCT (i.e., beyond the first 100 days post-HSCT). Hence, supportive interventions are needed to help patients manage and cope with the various challenges of allogeneic HSCT recovery, especially beyond the transplant hospitalization.

Besides distress, patients undergoing HSCT report low levels of positive psychological well-being (PPWB), which individuals use to appraise their lives and function well [11]. PPWB entails positive thoughts, emotions, and strategies such as optimism, gratitude, positive affect, life satisfaction, and the ability to flourish [11–13]. Although PPWB is associated with important patient-reported outcomes (e.g., QOL, physical activity) in diverse medical populations [14–16], very few studies have described PPWB in the HSCT population and its impact on clinical outcomes [17]. For example, Lee and colleagues showed that patients with high optimistic expectations prior to their transplant hospitalization have less mortality [18]. Also, Knight and colleagues highlight the positive association between optimism and enhanced immune response via improved day-to-neutrophil engraftment [19]. Hence, supportive interventions to help HSCT survivors cultivate and enhance PPWB may be especially relevant for this population.

Positive psychology (PP) interventions entail simple, deliberate, and systematic exercises (e.g., noticing and savoring positive events), which consistently promote PPWB in medical populations but are lacking in the HSCT population [20,21]. PP interventions are especially promising for the HSCT population because, in other medical populations, they have reduced distress [22,23], increased QOL [24], and promoted health behaviors, and can potentially buffer against symptoms of distress while promoting well-being. Additionally, PP interventions delivered remotely (e.g., via phone) by individuals with diverse training backgrounds, including psychiatrists, psychologists, social workers, nurses, trainees, and bachelor-level research staff, are feasible [24–28]. Hence, PP interventions are potentially scalable supportive interventions that can address the unmet mental health needs of patients undergoing HSCT [29–32].

Considering the potential impact of PPWB on overall well-being and clinical outcomes in the HSCT population [17], we developed a manualized tailored PP intervention called the **P**ositive **A**ffect in the **T**ransplantation of **H**ematopoietic Stem Cell (**PATH**) intervention for this population. PATH entails nine weekly, 1:1, 15–20-min phone sessions to improve psychological distress symptoms and QOL in HSCT survivors [29]. We used a single-arm proof-of-concept trial to refine the PATH intervention which allowed us to modify the PATH intervention for this pilot randomized controlled trial (RCT) [29]. The National Institute of Health (NIH) Stage Model for behavioral intervention development justifies the current pilot RCT (NIH Stage 1b) [33] for several reasons, including 1) to assess the feasibility of the refined PATH intervention based on patient feedback in the single-arm trial, 2) to ensure that any observed changes in outcomes based on the PATH intervention are not just due to the passage of time, and 3) to assess the feasibility of outcome measures' assessment in a larger efficacy trial. Hence, data from this pilot RCT will assist in optimizing the PATH intervention for content, dosing, delivery, and study procedures in preparation for a full-scale multi-site efficacy trial.

2. Methods

2.1. Conceptual framework

The conceptual framework for this study (Fig. 1) was guided by: our prior qualitative study describing PPWB in this population [34], a systematic review that showed links between

PPWB and outcomes in the HSCT population [17], prior PP intervention development studies in other medical populations [35–37], and the Broaden and Build Theory of Positive Emotions which suggests that PPWB increases patients' emotional and cognitive resources for problem-solving strategies and coping [38]. Hence, the PATH intervention may improve clinical outcomes (e.g., improved symptoms of depression and anxiety [39], QOL [20,26],) via improvement in self-management targets, including PPWB, coping, and physical activity (Fig. 1). Additionally, the PATH intervention offers (**A1**) evidence-based and tailored positive psychology exercises to enhance PPWB, including flourishing, meaning, gratitude, and positive affect, based on patient-reported preferences from our single-arm trial [40,41]; (**B1**) positive psychology skills to promote self-management strategies like coping and physical activity [35–37]; (**C1**) PPWB and self-management strategies which may impact each other in a bi-directional way [42]; and together (**D1**) may mediate the impact of the PATH intervention on improved anxiety and depression symptoms and QOL [22,43] as coping has been shown to mediate the impact of supportive oncology interventions on outcomes [44–46]. Overall (**E1**), as with other positive psychology interventions, the PATH intervention may also directly lead to improved health-related outcomes, including improved symptoms of anxiety and depression [39] and QOL [20,26].

2.2. Study design

The NIH Stage Model which proposes an iterative and systematic framework for intervention development in Stages zero through four, informed the PATH intervention development and guided our study design of this pilot RCT (NIH Stage 1b) [33]. First, we conducted qualitative (n = 25) [34] and proof-of-concept (n = 12) [29] studies (NIH Stage IA) to refine and tailor the PATH intervention to the specific unmet psychological needs of patients HSCT survivors with feedback from patients and a multidisciplinary group of stakeholders including researchers and clinicians who work with this population. The current pilot RCT (NIH Stage 1B) is among the first to establish the feasibility and preliminary efficacy of a positive psychology intervention in improving psychological distress and QOL for HSCT survivors to inform future efficacy (NIH Stage 2 and 3) and dissemination and implementation work (NIH Stage 4).

2.3. Participants

Eligible patients are: 1) adults (≥ 18 years old) with hematologic malignancies who received allogeneic HSCT at the Dana-Farber Cancer Institute (DFCI), 2) at least 100 days post-HSCT, 3) capable of speaking, reading, and writing English, and 4) able to consistently access a phone. Patients will be excluded if they received HSCT for benign blood conditions or underwent outpatient HSCT because the recovery trajectory and the psychosocial needs of these HSCT populations differ from those of patients undergoing inpatient HSCT [4,5,29,34]. Patients will also be excluded if they have medical, psychiatric, or cognitive conditions that their treating clinicians believe will prohibit their ability to complete study procedures.

2.4. Recruitment and enrollment

A clinical research coordinator (CRC) will approach patients for study participation during their 70–80-day post-HSCT appointment over the phone or in the clinic to assess interest in participating. Participants who are interested and meet eligibility criteria will undergo informed consent and be enrolled in the study. To improve the socioeconomic and racial/ethnic diversity of study participants, we will collaborate with institutional Inclusion, Diversity, and Equity offices to ensure the robust recruitment strategies of patients from these underserved backgrounds. Enrolled participants will receive an *Actigraph GT3X+* and MEMS Cap to assess baseline physical activity and immunosuppressant medication adherence, respectively. Additionally, consented participants will complete baseline assessments around Day 85–90 post-HSCT (i.e., before initiation of the PATH intervention at 100 days post-HSCT for those randomized to the intervention group). A CRC blinded to the group assignment will administer these assessments.

2.5. Randomization

We will randomize participants equally to the intervention or usual care control groups using permuted blocks of sizes two and four, stratified by the presence/absence of GVHD. We chose permuted blocks of sizes two and four to account for a relatively small sample size (n = 70) with a high likelihood of imbalances in sociodemographic and clinical factors when allocating patients between our two study groups. We will stratify by GVHD to ensure a balanced representation between the two study groups because allogeneic HSCT survivors with GVHD experience different recovery trajectories, QOL, and physical functioning than those without GVHD [47–49]. Further, the effect of GVHD treatment (e.g., systemic corticosteroids) on psychiatric symptoms such as mood and behavior may create imbalances between the two study groups [2].

2.6. The PATH intervention

The PATH intervention was developed after thoroughly reviewing the literature and theoretical frameworks on positive emotions and their impact on clinical outcomes [50,51]. In addition to the literature on positive psychology interventions in other medical populations, we completed a single-arm proof-of-concept study to refine PATH for the HSCT population [52]. Tailoring our intervention to the HSCT population entailed incorporating positive psychology activities which may resonate with HSCT survivors vs. other chronic medical populations [13,21,22]. For example, suggestions for recalling positive life events will include considering interactions with their caregivers and clinicians, suggestions for the gratitude letter will include but not be limited to writing a letter to stem cell donors, and suggestions for using personal strengths may consider highlighting perseverance given the long duration of the recovery period. We chose the timing of PATH based on the following: 1) findings from our prior qualitative studies, which highlighted patients' desire and need for more supportive resources after the 100-day post-HSCT timepoint [29,34], 2) limited supportive resources tailored to the unique needs of allogeneic HSCT survivors beyond their transplant hospitalization, and 3) HSCT survivors reporting high levels of distress (e.g., anxiety) in the first six-months following HSCT [4,5]. Importantly, as part of the intervention, we will highlight to patients that promoting

PPWB should not be confused with the tyranny of positive thinking (i.e., where patients feel compelled to think positively and may believe that failure to think positively is a character defect that can lead to poor clinical outcomes and disease setbacks) [11].

2.7. Positive psychology exercises

The manualized PATH intervention consists of three 3-week thematic modules (Table 1), with participants completing distinct exercises in a given module [40,41,53,54]. In the third ("integration") week of each module, participants will identify the most useful skills from that module. They will practice using those skills in daily life that week to gain experience with their use and encourage their sustained future practice. Integration weeks are critical given the focus on maintaining gains beyond the intervention period (i.e., at least 9 weeks after completing the intervention) and data suggesting that continued improvements in positive affect result in greater physical functioning [23,55]. The duration of the intervention was chosen to balance skill-building and acceptability [25]. Weekly PATH intervention phone sessions will last approximately 15–20 min.

2.8. Intervention procedures

Participants randomized to the PATH intervention will meet (via phone) with the study interventionist, a psychiatrist with extensive training in positive psychology intervention delivery, at 100 days (+/− 7 days) post-HSCT. During the initial phone call, the interventionist will provide an overview of positive psychology and the PATH intervention. The interventionist will also introduce the first PP exercise during the initial call and ask participants to complete the first exercise over the next week. Subsequently, weekly intervention calls will entail the following: 1) review of the prior week's positive psychology exercise (Table 1) with the participant exploring the impact of the exercise on their well-being, 2) discussion of how the PP skills can be used in daily life, and 3) introduction to the subsequent week's PP exercise via a guided review of the intervention manual and a discussion of the rationale of the exercises. All intervention group participants will be asked to complete all nine weekly PP exercises. Participants will complete the PP exercises independently during the week and will write about the activities and their effects before the call with the interventionist.

2.9. Training and fidelity

The study team will take several measures to ensure the fidelity of the intervention delivery. We will use rigorous training procedures for all interventionists managing the intervention delivery procedures. For the intervention delivery, we will use a well-established intervention guide successfully used in prior studies by our group and pilot-tested in this population [29]. To ensure fidelity of the intervention delivery, HLA will meet weekly with JH, an international expert in PP intervention development for patients with serious illnesses. JH will provide ongoing training on effective and consistent delivery of positive psychology exercises to participants and will help problem-solve any issues that may arise during the intervention delivery. We will also audio-record all sessions. Using a fidelity checklist developed from prior work, JH will review 10% of these recordings to ensure that all PP intervention sessions are delivered as described in the protocol and to

measure the extent to which the planned content domains of each session were actually addressed [21,22].

2.10. Usual care control condition

We chose a usual HSCT care control condition which entails as-needed 1:1 in-person meetings with social workers within the context of the routine care for HSCT recipients at the DFCI. All patients are required to engage in a one-time 1:1 in-person mental health assessment by a social worker before transplantation. The social worker is subsequently available to meet as needed with patients and their families throughout the post-transplant recovery period to connect patients with institutional and community resources to address their psychosocial needs. Social work assessments typically involve supportive care but do not focus on PPWB skill-building or cognitive strategies that promote positive emotions. Participants in the intervention group can also receive care from social workers as needed. We will track social work visits and other psychosocial support received by participants in both groups.

2.11. Study outcome measurements

Informed by our prior work and the conceptual framework for our study [17], we will use patient-reported outcome (PRO) measures with strong psychometric properties commonly used to assess psychological outcomes, QOL, coping, and health behaviors in our study population [7,9]. PRO measures will be assessed at the end of the intervention at 9 weeks to determine the immediate impact of the intervention and at 18 weeks to evaluate the sustainable effects of the intervention. We will send participants the PRO measures to fill out either electronically via a REDCap survey link or in person with a paper packet.

2.11.1. Sociodemographic information—We will obtain patient sociodemographic data via a self-reported questionnaire completed by study participants on age, sex, race, ethnicity, religion, relationship status, educational level, annual household income, and living situation.

2.11.2. Feasibility and acceptability (primary outcome)—Based on prior work, we defined feasibility as > 60% of eligible participants enrolling in the study and > 75% of enrolled participants in the intervention group completing at least 6 of the 9 PP sessions, consistent with metrics used in prior positive psychology feasibility trials [21,22] and other behavioral intervention studies [56–58].

We will assess acceptability using weekly ratings of the ease and utility of each exercise (0 = very difficult/not helpful; 10 = very easy/very helpful). Immediately after completing the weekly exercise and phone session, participants will rate the ease of exercise/session completion and the overall utility of the exercise/phone session with a 10-point Likert scale used in prior positive psychology intervention studies [19,57].

To obtain participants' immediate feedback on the impact of positive psychology exercises on optimism and happiness, we will use a 10-point Likert scale as in other positive psychology intervention trials [19,57].

2.12. Secondary outcomes

Psychological outcomes: We will assess positive and negative psychological states using validated measures in medical populations.

2.12.1. Positive psychological well-being assessments

Optimism: We will use the 10-item Life Orientation Test-Revised (LOT-R) to measure dispositional (trait) optimism (Cronbach's alpha = 0.874). Higher scores indicate greater optimism [59].

Positive Affect: We will use the 10-item Positive Affect Schedule (PANAS) to measure positive affect (Cronbach's alpha = 0.919). Higher scores indicate greater positive affect [60].

Life Satisfaction: We will use the 5-item Satisfaction with Life Scale (SWLS) to measure satisfaction with life (Cronbach's alpha = 0.893). Higher scores indicate greater satisfaction with life [61].

Gratitude: We will use the 6-item Gratitude Questionnaire (GQ-6) to measure dispositional gratitude (Cronbach's alpha = 0.735). Higher scores indicate greater proneness to experience gratitude in daily life [62].

Flourishing: We will use the 8-item Flourishing Scale to assess a person's self-perceived success in critical areas such as engagement, relationships, self-esteem, meaning and purpose, and optimism (Cronbach's alpha = 0.867). Higher scores indicate more psychological resources and strengths [63].

2.12.2. Psychological distress assessments

Anxiety and Depression: We will use the Hospital Anxiety and Depression Scale (HADS) to assess symptoms of depression and anxiety. The HADS is a 14-item questionnaire that contains two 7-item subscales assessing depression and anxiety symptoms during the past week (Cronbach's alpha = 0.826) [64]. Scores on each subscale range from 0 to 21, with higher scores indicating more symptoms of anxiety and depression.

Posttraumatic Stress Symptoms: We will use the Post-Traumatic Stress Disorder Checklist (PCL) to assess symptoms of post-traumatic stress. The PCL is a 17-item self-report measure that evaluates post-traumatic stress symptoms (Cronbach's alpha = 0.876) [65]. Higher scores indicate more symptoms of post-traumatic stress.

Quality of Life: We will use the 47-item Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) to assess QOL, validated for use in patients undergoing HSCT [66]. The FACT-BMT consists of five subscales assessing well-being across four domains (physical, functional, emotional, social, and bone marrow transplant symptoms) (Cronbach's alpha = 0.930). Higher scores indicate better QOL.

Coping: We will use the Brief Cope, a 28-item questionnaire that assesses 14 methods of coping (e.g., self-distraction, humor, denial) using a 4-point Likert scale (Cronbach's alpha = 0.755) [67].

Health Behaviors: Since PPWB is associated with increased physical activity and medication adherence in medical populations, we want to establish the feasibility of assessing health behaviors as part of the current study [25,26,35]. We selected physical activity and medication adherence as our two behavioral outcomes, with minutes/day of light activity (100–1951 counts/min [68,69]) and sedentary leisure time (SLT) [68,70] as our primary activity measures [71], given their links to health outcomes. We will use the well-validated Actigraph GT3X+ accelerometer [68] for seven days of wear. Minimum acceptable use is defined as 4+ days with 10+ hours of recorded data, as in prior guidelines [71–73]. We will use the electronic pill monitoring system, MEMS Caps [74], to electronically monitor immunosuppressant adherence throughout the study, along with patient self-report and electronic health records. We will determine immunosuppressant medication and dosing and calculate changes in adherence over time (% of medication correctly taken, by week and month) based on MEMS data. Additionally, we will assess self-reported adherence to Tacrolimus, Sirolimus, or Acyclovir with the Medication Adherence Scale-5 (MARS-5), a self-report adherence measure used extensively in medical populations [75,76].

2.13. Statistical methods

We will use descriptive statistics (e.g., median, variance) for all continuous variables and proportions for all categorical variables in characterizing participant characteristics. All statistical tests will be two-tailed; $p < 0.05$ will be considered significant.

2.13.1. Feasibility and acceptability

Feasibility is the primary outcome of this study.: We will estimate the feasibility using the proportion of eligible patients who enroll in the study and place an exact 95% binomial confidence interval around the proportion. The mean ease and utility of each exercise will be calculated, and we will compare these means to a mean combined score threshold of 7.0/10 for acceptability used in prior studies [19,57].

2.13.2. Secondary outcomes—To examine participant's subjective report on immediate impact of the intervention on happiness and optimism, we will use generalized estimating equations (GEE) to determine the immediate impact of the PP exercises on optimism and happiness. The GEE model will allow us to account for the repeated observations of participants from the different weekly PP exercises.

For all PRO measures (i.e., optimism, satisfaction with life, gratitude, positive affect, flourishing, depression, anxiety, PTSD symptoms, QOL, and coping), we will compare between-group differences in change over time at the 9 (i.e., primary endpoint) and 18-week time points using random-effects regression models with a random intercept for each patient. These analyses will include all time points, and our models will have a categorical effect of time (i.e., baseline, week 9, and week 18), a group effect, and a time-by-group interaction.

The time-by-group interaction will estimate the difference in the change from baseline to each time point, and these regression coefficients were the focus of the analyses. Data from all three time points will be included.

For behavioral outcomes (i.e., medication adherence, physical activity), we will compare physical activity (# of steps/day) at baseline and 9 weeks between the intervention and control groups using *t*-tests or Wilcoxon rank-sum tests, depending on the distribution of the variables. We will also use random-effects regression models with a random intercept for each participant to compare between-group differences in changes in physical activity and medication adherence over time.

Given the pilot nature of the study, we did not power the study to detect statistically significant group differences. We will examine differences in the change with time and sample variance components on the secondary outcomes. We will calculate effect sizes (Cohen's d) for changes in outcomes from baseline, weeks 9, and 18 [77]. The effect sizes will be used to estimate the necessary sample size to conduct a future full-scale efficacy trial with power > 80%. We will also verify the sample size by detecting a clinically meaningful difference and referencing existing literature [78]. From this pilot study, we will determine the minimum clinically meaningful difference in outcomes, for example, anxiety and depression symptoms based on the HADS. We will ensure that our effect size is greater than the minimum clinically important differences in the outcome measures equivalent to or superior to other supportive oncology interventions for the HSCT population.

2.13.3. Missing data—We will use the intention-to-treat (ITT) principle with all randomized participants contributing to the primary analyses even if they do not adhere to the intervention. We will also conduct sensitivity analyses to explore various assumptions about missing data. If the source of the missing data appears to be random, the linear mixed-effects models described above will provide an unbiased estimate of the regression coefficients. In addition to the intention-to-treat analysis, we will also estimate the group differences in the completers to estimate the per-protocol group difference.

2.13.4. Power consideration—Based on prior trials in this population [8], we anticipate that 15% of enrolled participants might not complete the intervention due to medical complications and mortality. Hence, we will enroll 70 participants (35 in the intervention group) to target having at least 30 participants who are eligible to complete the intervention. In prior trials, approximately 80% of participants have completed 6 of 9 PP exercises [23]. Using the same rate, with 30 intervention participants, we will have 95% power (two-sided $\alpha = 0.05$, binomial proportion test) to demonstrate that the proportion who will complete > 6 of 9 PP sessions will be larger than 50%. For acceptability, using this sample size, we will have 95% power to detect a true mean score of > 7.0 based on prior work (in which mean utility scores were 7.8 +/− 1.8) [79].

This pilot study was not designed to definitively detect statistically significant ($p < 0.05$) group differences in psychological, QOL, or behavioral outcomes (and we would need between-group effect size differences of $d = 0.74$ to be powered at 80% to detect significant differences). The effect sizes were guided by our proof-of-concept study of

the PATH intervention, which led to very small-to-medium effect size improvements in patient-reported outcomes such as optimism, positive affect, symptoms of depression and anxiety, quality of life (QOL), and fatigue [29].

3. Discussion

With the high burden of psychological distress, QOL, and functional deficits among HSCT survivors, more supportive resources are needed for this population. We provide a comprehensive overview of how a feasibility pilot RCT of a novel positive psychological intervention, PATH, will be carried out in HSCT survivors at 100-days post HSCT and beyond. To our knowledge, this is the first RCT of a PP intervention in the HSCT population. Hence, our work can potentially guide others working on similar interventions in this and other oncological populations.

This RCT will provide important information on intervention dosing and duration that would be tolerable in a population with significant physical and psychological symptoms. Prior PP interventions in other medical populations have consisted of 8–12 weekly sessions [35–37], and other supportive interventions for hospitalized HSCT recipients have entailed 6–8 modules [7]. Our study will show whether the HSCT population can tolerate and engage in a 9-week intervention outside the hospital [35–37]. Although our sample size is not powered to determine the impact of the intervention on PROs, our preliminary longitudinal analyses will provide insights on which PROs to further explore in larger efficacy trials.

Positive psychological interventions like PATH may be especially relevant for HSCT survivors and other vulnerable, seriously ill patients for several reasons. First, it has the potential to fill a gap in psychosocial support resources during a vulnerable period in HSCT care (i.e., 100-days post-HSCT) when patients are starting to have less frequent touch points with their HSCT clinicians compared to existing interventions which primarily target the HSCT hospitalization [7–10]. Second, PATH may be more accessible and easily scaled since it phone-based and can be successfully delivered by non-specialty mental health clinicians [7–10]. Third, PP interventions have successfully enhanced well-being, health behaviors (e.g., physical activity), and clinical outcomes in several medical populations [23,24,35,37,79]. Thus, interventions like PATH may yield short- and long-term health benefits for the HSCT population.

Our study has several limitations for consideration. First, our study will be performed at an academic cancer center with one of the largest HSCT programs in the world. Hence, feasibility and acceptability data from a robust cancer program with supportive resources may differ from smaller and community programs with limited psychosocial services. Second, our sample size of 70 will not allow us to make robust assessments about intervention impacts on PRO. Hence, larger efficacy trials would be needed to establish the impact of a PP intervention like PATH on PROs in this population. Third, our intervention for this pilot study will be delivered in English and not accessible to non-English speaking patients with significant unmet psychosocial needs. Hence, larger efficacy trials should consider translation to other languages commonly used in the United States, like Spanish, to determine how the intervention impacts among non-English speaking patients.

In summary, this RCT of a PP intervention for HSCT recipients provides important preliminary information for designing and implementing similar interventions in vulnerable cancer populations with significant physical, psychological, and recovery needs, such as the HSCT population. If the PATH intervention is feasible, the next step will be to test the PATH intervention in large randomized controlled efficacy trials in diverse populations.

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Data availability

Data will be made available on request.

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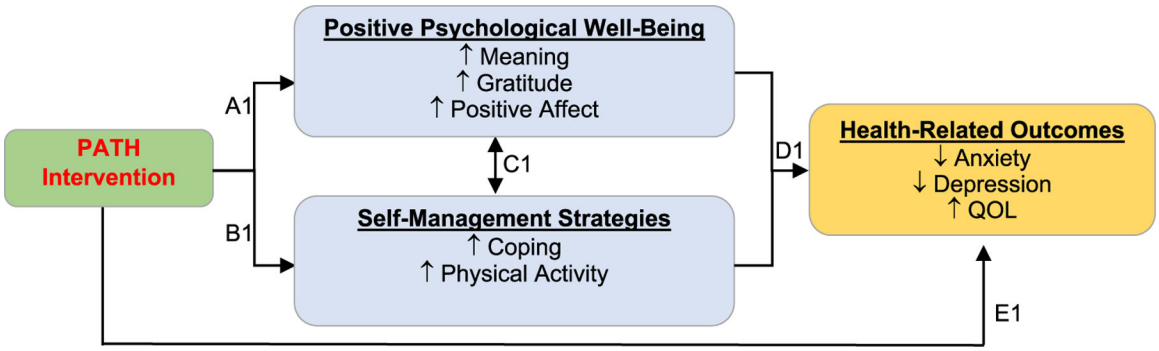

Fig. 1.
Conceptual model.

Table 1

The PATH intervention components.

Module 1: Gratitude/positive affect-based exercises		
Week 1	Gratitude for positive events [43]	Participants identify three positive events that have occurred in the past week and reflect on their feelings as they recall and describe these events.
2	Gratitude letter [43]	Participants write a letter of gratitude thanking a person for their support or kindness.
3	Gratitude skills application	Participants select a useful activity from the prior two weeks, consider how to adapt the activity to daily life, and develop a plan to utilize this skill regularly.
Module 2: Strengths-based exercises		
Week 4	Recalling past success [44]	Participants recall an event in which they experienced success, then write about the event, their contribution to the success, and the positive feelings elicited by recalling it.
5	Using personal strengths [43]	Participants undergo a brief assessment of personal strengths, then find a new way to use one of their ‘signature strengths’ in the next 7 days.
6	Strength-based skills application	Participants select a useful activity from the prior two weeks, consider how to adapt the activity to daily life, and develop a plan to utilize this skill regularly.
Module 3: Optimism and meaning-based exercises		
Week 7	Enjoyable and meaningful activities [59]	Participants complete three activities: an enjoyable activity alone, an enjoyable activity with another person, and a meaningful activity completed alone or with others.
8	The good life [60]	Participants imagine and write in detail about the best possible (realistic) future one year from now and consider small short-term steps to take toward such a future.
9	Skills application + future planning	Participants select an activity from this module and develop a plan to utilize this skill—and additional skills from the program—this week and beyond