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INSPIRE: A Multicenter Randomized Controlled Trial integrating health informatics in a scalable stepped care self-management program for survivors after hematopoietic cell transplantation

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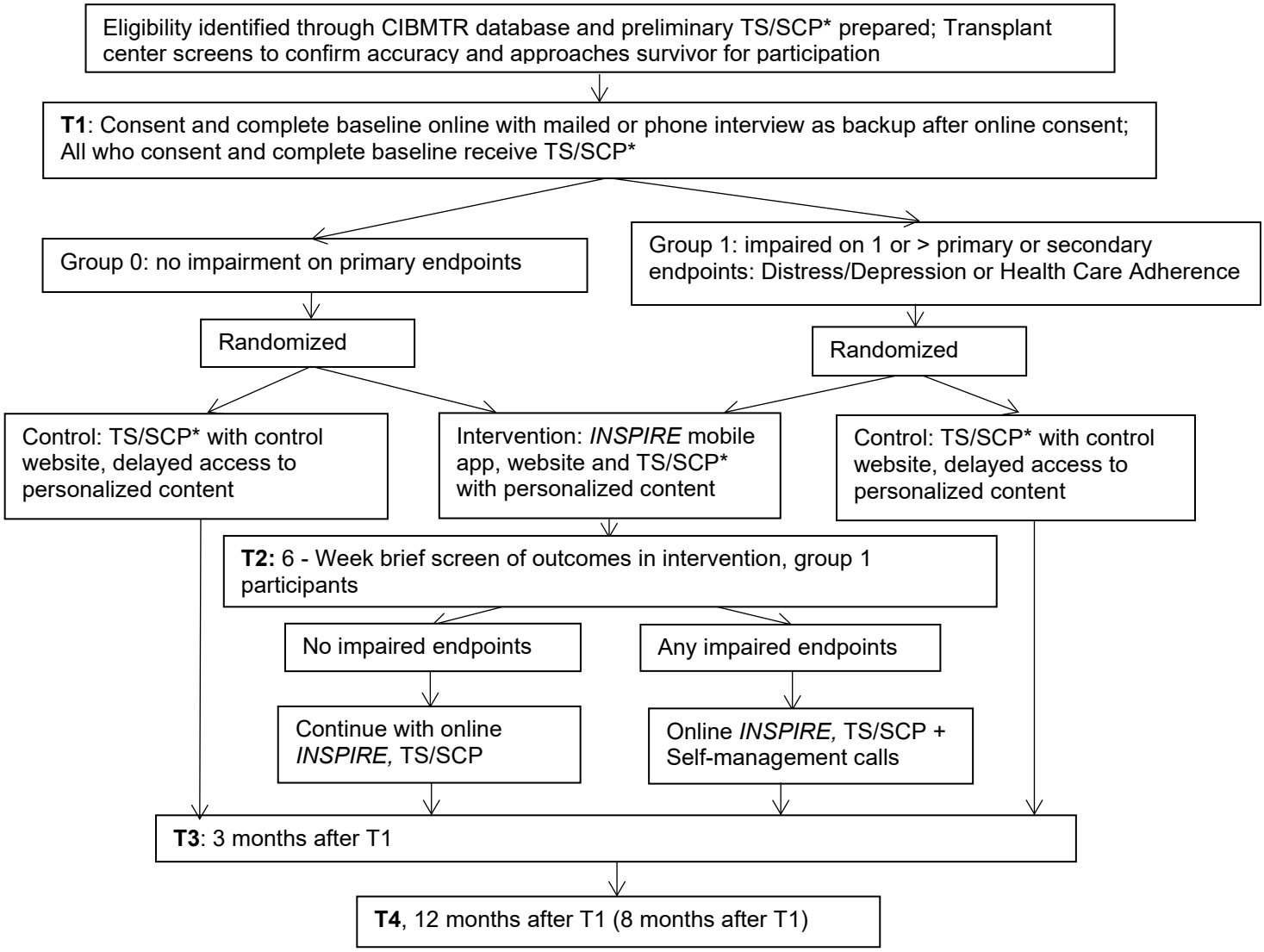
TABLE OF CONTENTS

STUDY SCHEMA: Phase III Multicenter Randomized Controlled Clinical Trial



* TS/SCP = treatment summary and personalized survivorship care plan given to all intervention and control study participants.

1.0 INTRODUCTION

This document is a Phase III clinical research protocol and the described study will be conducted in compliance with the IRB approved protocol, associated Federal regulations and all applicable IRB requirements.

This study proposes that predictable health surveillance and unmet emotional needs of adult hematopoietic cell transplantation (HCT) survivors can be improved through a centralized, cost and resource-sparing, national program that optimizes health informatics and provides online expertise and stepped care telehealth assistance with using the program when necessary. If successful, this project would provide long-term HCT survivors and their providers with a patient-centered program to facilitate managing their emotional and health care needs. Long-term HCT survivors do not receive adequate care for their unique health and emotional needs due to lack of knowledge and resources to manage these needs in their home communities, although many of these needs have been well defined. Lack of access to care increases premature morbidity and mortality in HCT survivors particularly for cardiovascular and metabolic disease (cardiometabolic) and subsequent malignancies.

Among adult long-term cancer survivors, those who received HCT have a 9-fold increased risk of mortality related most commonly to cancer recurrence, subsequent malignancy s and cardiovascular diseases.[2-5] They are also at risk for poorer psychosocial health including cancer-related distress, with depression at higher levels than age-matched norms.[6-8] By focusing on HCT survivors who are 2-5 years after treatment, we target a high risk group and build upon our previous experience delivering tailored online content with telehealth/phone based stepped care for those who do not improve at an interim assessment point at 6-weeks after randomization.

The major goal of this protocol is to test the efficacy of the integrated, tailored online site, using a self-management model of care that distributes survivorship care plans, tools and resources for management of distress and health care adherence directly to cancer survivors as the coordinators of their own health. Our previous research has demonstrated efficacy in reducing depression and distress with survivors at a single site[9, 10], at six sites across the nation[11], and has tested the efficacy of providing a survivorship preventive care plan{4855}[10] With this protocol we will retain the focus on depression, distress and health behaviors, while improving the methodology by adding telehealth stepped care and leveraging the data registry and assessment infrastructure at the Center for International Blood and Marrow Transplant Research and the National Marrow Donor Program (CIBMTR/NMDP) for post-study sustainable implementation of the program. The protocol also builds on increasing recognition that a single online device or method will not meet the needs of all survivors.

Although HCT is often considered distinct from other cancer treatments, the primary outcomes in the proposed research are also some of the most prevalent concerns and causes of mortality in other groups of survivors treated with standard therapy.[12, 13] The methods we propose are relevant for any survivors who would benefit from cost and resource conserving interventions provided by online and telehealth modalities. With these improvements and the extension of the intervention to twelve transplant centers we expect to strengthen both the reach and efficacy of the intervention tested in protocols 2258 and 2605, while we advance the science of delivering health behavior change models of care to cancer survivors.

This protocol is a 12-site multicenter RCT (N=492), with Seattle as the prime site, partnering with transplant centers in Ohio, Minnesota, Wisconsin, Michigan, Massachusetts, Pennsylvania, New York, Florida, Kansas, Illinois, and Texas. This provides age, region and rural/urban diversity. Participants randomized to the intervention will receive immediate access to the tailored online program, with options for social-media, adding stepped care self-management calls for those not improving by a 6-week interim assessment for those in group 1. Control participants will receive access to a website that provides annotated links to publicly available HCT and cancer websites as well as delayed internet site access. Outcomes will be assessed at 6 weeks, 3 months and 12 months.

2.0 BACKGROUND

Among adult long-term cancer survivors, those who received HCT live with some of the highest risks for life-threatening chronic health conditions including cardiovascular disease, diabetes, osteoporosis, and recurrence or second cancers along with other risks. Even more prevalent in HCT survivors are psychological symptoms that inhibit quality of life, specifically depression and cancer-related distress. Many survivors have residual complications in specific domains with resultant impact on quality of life (QOL.)[14]. Survivors have more difficulty after transplant if they struggle with chronic GVHD, have pulmonary disease, infection or other psychological or medical complications. [15-17]

Significance and Gaps This Project Will Fill

Despite their rapidly expanding numbers, survivors more than 5 years after HCT have been understudied both in defining their needs and in addressing long term complications through RCTs. This protocol extends our knowledge of long term or late effects while testing treatment to reduce common problems that have not resolved on their own. A major impediment to addressing needs of HCT survivors is their dispersion around the country, in areas lacking transplant-related expertise. Online methodologies will allow us to enroll difficult to access survivors and will provide otherwise unavailable expertise and evidence-based guidelines for care. With this internet, social-media and telehealth program, we optimize flexibility to respond at the readiness and at the time convenience of participants in a highly cost-effective modality since adding participants adds minimal cost. We believe the program could improve standards of care and health outcomes for HCT survivors and address a major gap in care for these geographically dispersed survivors.

Cancer-Related Emotional Distress and Depression. Cancer-related distress is a significant problem for HCT and other with a negative impact on quality of life.[6, 18] Distress is far more prevalent than clinical depression, with prevalence estimated at 43% in long-term HCT survivors and moderate to severe depressive symptoms in 13-15%.[7, 19-21] Distress can be due to many factors such as uncertainty, cGVHD, managing the side effects of transplant, and financial stress.[22-24] Our preliminary research found that 41% of 2-5 year HCT survivor study participants had elevated distress on the Cancer and Treatment Distress (CTXD) measure.[25] In the cohort of 936 study participants, all but 1% of those with elevated depression scores also had elevated distress on the CTXD, suggesting that the CTXD captures a large proportion of depressive symptoms.[11] Therefore, we believe our focus on CTXD distress as the primary outcome will also address depression needs for nearly all survivors, although we will still measure depressive symptoms as a secondary endpoint. Risk factors for distress for allogeneic HCT include younger age, shorter time after HCT, and cGVHD. For autologous HCT, comorbidities are a risk factor for distress.[26, 27] Pre-HCT depression predicts later depression and other poorer outcomes[6, 27] as well as survival.[6, 28, 29] We have demonstrated that the INSPIRE online program for HCT survivors can improve distress (see 2.2 Preliminary Research). Others have demonstrated improved distress and post-traumatic stress in HCT survivors with telehealth cognitive behavioral treatment.[30]

Cardiovascular Disease (CVD) and Metabolic Syndrome. With a risk of premature CVD related death increased 2.3- 4.0-fold compared to the general population,[31, 32] HCT survivors are more likely to develop adverse CVD risk factors leading to development of metabolic syndrome (constellation of high triglyceride levels, low HDL-cholesterol, hypertension, high fasting glucose and increased waist circumference) which predisposes individuals to early CVD-related death. Insulin resistance is the primary pathophysiologic mechanism and HCT survivors are more likely to develop hypertension, hyperlipidemia, and diabetes.[33-36] In the Bone Marrow Transplant Survivor Study we examined diabetes, hypertension, and CVD events in 2+ year HCT survivors (n=1089) and found that allogeneic HCT survivors were 3.6 and 2.0 times more likely to report diabetes and hypertension compared to siblings. In addition, exposure to TBI increased the risk of diabetes 3.4 times.[37] In a case-control study of 1379 HCT survivors compared to 509 randomly selected individuals from the general population, the 10-year cumulative incidence of ischemic heart disease, cardiomyopathy, stroke, and all-cause death from CVD ranged from 3.5-6.0%.[38] Other mechanisms include cardiomyopathy and coronary artery damage due to chemotherapy and chest irradiation.[38-43] Most cardiometabolic abnormalities can be screened for and treated. Screening and preventative recommendations for CVD in HCT survivors have been recently published by a combined US and European task force.[44]

Subsequent Malignancy Risk. As the leading cause of non-relapse late mortality, subsequent malignancy s after HCT are one of the most significant long-term health risks. Numerous studies report the risk of a subsequent malignancy between 4 to 11-fold higher than in the general population.[45-51] The types of subsequent malignancy s seen vary over time with earlier occurrence for myelodysplasia/acute myeloid leukemia and post-transplant lymphoproliferative disorders and longer latency for solid tumors.[52] The cumulative incidence of subsequent malignancy s increases with longer length of follow-up, approaching 8.8% at 20 years after HCT, and no evidence of a plateau.[49] Risks of subsequent malignancy s after HCT are increased for skin, thyroid, oral cavity, esophagus, liver, breast, nervous system, bone and connective tissues,[46-48, 53] and risk factors include total body irradiation (TBI), young age at HCT, cGVHD and prolonged immunosuppression.[54] HCT survivor specific guidelines have been published taking these into account,[54] and form the basis for the recommendations in the SCP that will be utilized for this study.[55-58]

Treatment Summary & Survivorship Care Plan (SCP). SCPs are recommended for all cancer survivors, and should include the following information: (1) cancer type, treatments and their potential long term effects, (2) information about screening and preventive evaluations and their timing, and (3) recommendations about lifestyle practices.[59, 60] When used in shared decision making as a cornerstone of self-management, SCPs may increase communication between oncologists and primary care providers.[61] A majority of cancer programs face barriers to implementing delivery of SCPs (time and effort to create and disseminate) and thus are not providing them.[62-66] Having a written plan may help survivors more than just talking with them about their SCPs.[67, 68] Health informatics reduces barriers to generating SCPs.[69, 70] We are designing this protocol with dissemination in mind as has been recommended when using SCPs.[71] To date, research testing delivery of a printed SCP, without follow-up to personalize the application of the information to the individual, has not found positive outcomes with regard to health care adherence (HCA) or distress, although survivors may report feeling positive about having received SCPs.[65, 72-84] Personalizing an action plan for the individual through online interaction, and follow-up to address barriers by telehealth if needed, are necessary to make SCPs more effective.[85, 86]

Preliminary Research

Preliminary Studies that Provide a Foundation for the Planned Methodology

The scientific premise of the study builds on our preliminary research and work done in other chronic conditions such as diabetes that supports the value of online and telehealth self-management. Online interventions for chronic diseases have proliferated, with mixed and at most modest success.[87-89] Effect sizes are modest at best since those with greater problems are less likely to engage with the program.[90] Other than our INSPIRE study, only 2 interventions we are aware of with HCT populations have reduced distress and depressive symptoms; those required cognitive behavioral treatment delivered over the phone or in person.[30, 91] Online programs are an attractive option for HCT survivors as many live far from their transplant center, and many go online for information.[92-95] Social media provides access to other survivors through private groups and has been used in interventions with non-HCT cancer survivors with some success.[96-98] A major limitation of online interventions is that many who sign up are already doing quite well in their health behaviors.[99, 100] Literature search indicates few published RCTs of online interventions in cancer survivors, with mixed findings.[88, 101] While a few interventions have been found to be efficacious,[102-108] the effect sizes are small and published studies tend to focus on feasibility and acceptability and not outcomes or efficacy.[69, 109-117] Studies that provide options for participants to write content and complete action plans as part of the intervention have better outcomes than those where participants just read.[118] This interactivity is an effective component of online interventions.[87, 119, 120] We propose to strengthen the proven online intervention from our INSPIRE multicenter RCT by creating a responsive design for use on all platforms, including social media, which will allow increased interactive options and improved personalization of the content.[121]

PCORI-SCP Study

This study had two phases; the first involved focus groups of HCT patients/caregivers and providers involved in survivorship care to get feedback on a SCP template and its implementation using the

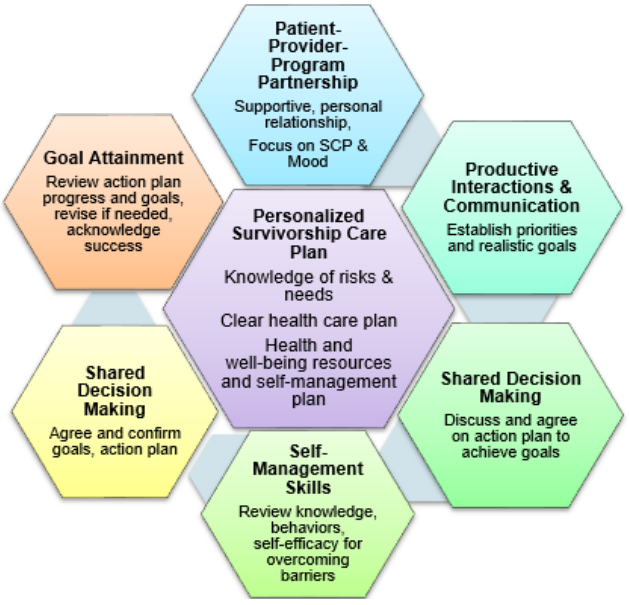
centralized CIBMTR registry. This qualitative research led to a final patient-centered SCP instrument that incorporated relevant clinical information from CIBMTR data and recommendations for screening and prevention of late effects based on specific exposures identified by the international long-term follow-up guidelines for HCT survivors (guideline effort led by Dr. Majhail).[122-124] The final SCP is being tested in an ongoing RCT that compares usual care to the personalized SCP in HCT survivors 2-5 years post-transplant. Endpoints include patient survivorship confidence in knowledge, HCA, health behaviors, and HCT-related emotional distress at 6-months after the intervention. As of June 2016, 464 of the planned 495 HCT survivors have been enrolled through 17 transplant centers. The PCORI-SCP study has laid the foundation and infrastructure for this project with CIBMTR/NMDP, the investigators and the SCP. To strengthen the potential effect size of the SCP intervention, we will directly send the SCP to providers because studies have shown that reliance on survivors alone to disseminate a copy of their SCP to their provider is problematic.[69, 125] Overall, interventions that give materials to both patients and providers have been more effective in general population studies that seek to improve overall adherence to recommended preventive care.[126, 127]

INSPIRE Studies

We have completed 2 INSPIRE RCTs (protocols 2258 and 2605), improving feasibility and implementation of the program while refining procedures for study administration across multiple sites, personalizing approach to survivors through informatics programming, and with a change in primary outcomes to focus on adherence. In our first INSPIRE study we administered the online program targeting primary outcomes of depression, distress and fatigue, without personalized content but with a 3-group randomization including a 'standard care' control arm, the online intervention, and the online intervention plus a Problem Solving Treatment (PST) administered with 8 phone calls.[10, 128-130] Fred Hutch HCT survivors 3-18 years after HCT were eligible. Participation rate was 58% for those eligible and approached, with those age <40 years, non-white races, and >10 years after HCT less likely to enroll.[128] Once randomized to intervention, 77% logged in at least once and pages viewed did not differ by race, ethnicity, education, income, computer experience, donor type, healthcare adherence, distress or depression, but those likely to view 3+ pages of the site were more likely to be over 40 years and female. We found no efficacy for fatigue but did find important outcomes for distress and depression. For those who were impaired we found twice the rate of improved distress in those randomized to the intervention. Distress was more likely to improve in those age 40+ and in those <10 years after HCT[10]. From these results, we designed the next multicenter INSPIRE study to address shortfalls. Given the incremental improvement relative to large resource requirements to administer the 8-session PST with masters or doctoral level trained clinicians, and lack of interest in the number of sessions by many participants, we did not retain PST in the next study.

Our most recent multicenter INSPIRE RCT (CA160684) provides a platform and infrastructure for this study. The project approached N=2653 screened survivors 2-10 years after HCT at 6 national transplant centers, and enrolled 1064 survivors using the eligibility criteria as planned for this protocol. Of these, 470 had impairments on one or more primary endpoints of depression, distress or overall HCA. Final 12-month outcomes were completed in December 2016, and analyses are in process. In examining reach of the entirely online INSPIRE program with social media, participation did not differ by ethnicity, urban/rural residence, transplant intensity, or diagnosis, but was more likely for women, allogeneic HCT recipients, and age 40-60[11]. We conclude that strategies are needed to improve reach to men, younger and older adults. We designed this intervention to better target engagement and meet the personal needs of these subgroups. Preliminary analyses of 3-month outcomes indicate efficacy of the intervention for distress in those who access the online intervention. We see no interaction of intervention arm

FIGURE 1. Survivorship self-management model (adapted from McCorkle and Colleagues, CA Cancer J Clin. 2011.)[1].



outcome based on sex, age, race or time since HCT. However, viewing the online site interacts significantly with randomized intervention, indicating significantly higher rate of improvement for intervention recipients who engaged.

Self-Management Theory

Self-Management has been used to help patients cope with their chronic diseases (e.g., diabetes) and has been influencing cancer survivorship.[1, 90, 95, 131] Foster and colleagues developed an online intervention to assist survivors in self-managing fatigue.[132] Self-management has been used in cancer survivors to increase physical activity and improve diet,[133] and to reduce distress.[134] In a meta-analysis of online self-management studies, small to moderate effect sizes were found for anxiety, depression and quality of life.[89] Younger survivors expect that at least some of their self-management will occur online.[135] Self-management is a central premise of online interventions that attempt behavior change (see Figure 1.2 for our planned model of self-management).[136]

Stepped Care Using Telehealth. HCT survivors are amenable to using telehealth calls.[30, 137] One stepped care intervention was found to be comparable to usual care, but the study was done in the pre-transplant setting and enrolled patients with low distress.[138] Telehealth has been as effective as face-to-face interventions for cancer survivors.[139] Our first INSPIRE program found that PST using 8 phone calls in addition to the online intervention, compared with the online program alone or delayed access control, was more effective than online alone for distress.[10] However, we found great variety in the chosen targets for PST, such that it was difficult to measure outcomes, and many survivors did not feel a need for the extended telehealth calls. For the stepped care methodology, we are using a self-management model we have tested with young adult cancer survivors, with 3 phone calls and content focused on achieving goals specific to the study endpoints of distress, cardiac and/or subsequent malignancy HCA, and retaining an emphasis on specifying personal goals and anticipating barriers and facilitators to reaching goals.

This protocol tests an intervention to reduce common problems after HCT that have not resolved by two years after treatment, while extending our knowledge of risks for long-term or late effects in these survivors. It builds on prior online intervention research, with broad reach and high utilization. If efficacious in this multi-center RCT, it can be disseminated nationwide with limited maintenance costs.

3.0 OBJECTIVE

To determine the efficacy of a multicenter RCT of a self-management survivorship intervention that includes a personalized mobile application that is cross-device enabled, with internet and social media options, including stepped care telehealth, for adult 2-5 year HCT survivors enrolled from national transplant centers.

Primary Aims

1. Determine whether 2-5 year HCT survivors with elevated cancer-related distress or poor health care adherence, adherence to cardiometabolic or subsequent malignancy surveillance who are randomized to receive the online, patient-centered, self-management stepped care program will report reduced distress, and improved health care adherence for cardiometabolic or subsequent malignancy surveillance at 12 months when compared with an active control group who receive access to HCT survivorship best practices.
2. Determine characteristics of intervention participants who require telehealth stepped care at 6-weeks because they 1) do not meet criteria for adequate knowledge of subsequent malignancy and cardiometabolic risks, or 2) do not report improved distress, or 3) have not logged in to the online program.
3. Determine resources that would be needed to sustain the intervention as a national HCT survivorship program if implemented through the CIBMTR//NMDP.

Secondary Aims

Secondary outcomes will include process measures of internet study reach and utilization, as well as depression, physical function, and knowledge of survivorship needs in HCT survivors.

4.0 SUBJECT SELECTION

Inclusion Criteria

4.1a Received ≥1 autologous or allogeneic (related or unrelated) HCT with curative intent at a participating transplant center for a hematologic malignancy.

4.1b Age 18 years of age or older at last transplant.

4.1c Survival 2-5 years after last HCT when first approached for enrollment.

4.1d In remission at time of study entry, may be receiving chemoprevention.

4.1e Internet and email access.

4.1f American and Canadian citizens, and/or those with mailing addresses in the US/Canada and/or temporarily residing anywhere outside the country (IE – military).

Exclusion Criteria

4.2a Development of invasive subsequent malignancy after HCT other than non-melanoma skin cancer, in the past two years.

4.2b Medical or other issue prohibiting computer use, reading or ability to comply with all study procedures or unable to communicate via phone (e.g., significant vision, hearing or cognitive impairment, major illness, hospitalization).

4.2d Residing in an institution or other living situation where health care decisions are not made by the participant (e.g., hospitalized, prisoners, living in a rehabilitation facility).

4.2e Does not complete baseline PRO assessment items required to determine stratification or whether the survivor meets inclusion and exclusion criteria.

4.2f Non-proficient in English (written and spoken).

5.0 EVALUATION, INFORMED CONSENT OF SUBJECT, AND SECURITY

After consortium transplant centers have gone through their individual processes to confirm participant eligibility to participate in INSPIRE and participant contact information, the sites will approach survivors treated at their facility with two letters, sent approximately two weeks apart with three phone calls in between, that include study information and a request for consent to communicate the survivors' contact information to NMDP and to the Coordinating Center at the Fred Hutch. Survivors can indicate interest in the study by returning a signed response form attached to the consent letter indicating that they permit their contact information to be sent to NMDP/Fred Hutch, or by calling their transplant center Study Coordinator, calling the study toll-free phone line directly, emailing the study-specific address (inspire@fredhutch.org), or going directly to the study URL (inspire4survivorship.org), entering their unique temporary study ID listed on their letter and signing up directly on the secure study internet site registration page where they can consent, provide registration information and setup their account. If survivors provide permission for NMDP/Fred Hutch study staff to contact them by signing and returning their mailed response form to the consortium sites, by calling study offices, or by giving verbal permission for study contact over the phone to the consortium sites, NDMP will contact the survivors and discuss protocol consent details with them.

Participants who express interest in the study after a phone call or email communication with NMDP will be sent an email with a link to the study secure URL. There they can enter their unique study ID, which will link

them into the secure site where they can register. Participants will have a choice to register with either an email and password of their choosing, or by using their login information associated with their Facebook or Amazon account. Once registration is complete, participants can sign the consent form. The consent, which includes HIPAA content, will be electronically signed online within the secure study registration site. Survivors will be able to review and print the consent document before signing or downloading a pdf of the consent. A blank version of the consent is also accessible at all times on the website. If survivors have questions or concerns before signing the consent, we encourage them to contact the study at the toll-free phone line or by email to the study address. Consent will be obtained using forms approved by the Institutional Review Board of the Fred Hutch, and the Coordinating Center will establish IRB Authorization Agreements with each of the consortium centers. Potential participants at these centers will not be contacted for enrollment eligibility until the center has IRB Authorization Agreements in place. All substantive modifications to the consent will follow the same procedure of securing IRB approval at the Coordinating Center.

If survivors have indicated interest but have not registered or logged in to register, NMDP Study Coordinators will contact survivors with reminder emails and phone calls for six weeks to find out whether any issues can be addressed to facilitate registration.

Survivors may submit emailed questions, comments or requests at any time to study staff. They also may call the toll-free study phone line and their call will be returned within 2 business days.

Internet Login Security

The internet site entry page after randomization will require the participant to login, with either an email and password of their choosing, or by using their login information associated with their Facebook or Amazon account. After initial study login, participants will have the option to place a cookie on their computer for the internet program future access without a password, but full login security will be in place during online assessment phases of the study. Once a patient is signed into the INSPIRE application, they will go directly to their survey during the survey window until the survey has been completed. We have used the process for a patient to create their own user name and password similarly in two previous INSPIRE RCT studies with internet security review and approval at the six previous study sites and with no problems detected.

6.0 SUBJECT REGISTRATION

Subjects will be assigned to the protocol by the Fred Hutch Study Coordinator, who will register the patient with the Fred Hutch Data Management Office (206-667-4728). Since consent occurs only through the study website, which is managed by the Coordinating Center, the participating consortium centers will not be involved in subject registration. After the eligible subjects have been registered, subjects will be randomized by the Fred Hutch Data Management Office (DMO), Monday through Friday between 8:30 and 4pm PST/PDT. The DMO will email the randomization assignment back to the Project Manager at the Coordinating Center. The DMO can be paged, if necessary, at 206-995-7437. The Project Manager will receive the randomization assignment. She will input the randomization arm into the databases to trigger the programmed website access (intervention or control) for the participant, and will email participants their link to the study site.

7.0 PLAN OF TREATMENT

Intervention Selection and Approach

The CIBMTR data registry contains 3765 potentially eligible 2-5 year survivors including 14% minorities from the 13 participating centers. The study Biostatistician will develop a Statistical Analysis Software (SAS) program for random selection of potentially eligible participants with oversampling of minorities (initially all eligible minority cases will be approached) until a minimum of 15% of those randomized are minority race or

ethnicity. The remaining non-minority survivors will be randomly ordered. Each participating center will be sent their randomized approach lists in blocks of 25 cases. Based on our previous INSPIRE enrollment experience with similar eligibility, we found that 26% of cases were not eligible after further screening. We project that we will enroll and randomize 51% of eligible non-minority survivors and 40% of minority survivors. Thus we expect we will approach approximately 1358 (36%) of potentially eligible cases, with 26% not eligible after approach, to achieve our total projected enrollment N=492 to the randomized study.

First contact will be made with a letter of approach from the site PI and Study Coordinator. The letters of approach from the consortium sites will request permission to provide contact information to NMDP as the follow-up coordinators and to Fred Hutch as the Coordinating Center. Survivors who have opted out of contact or are lost to follow-up will not be approached either by the Coordinating Center or consortium sites. In the order designated by the program from the study biostatistician until enrollment goals are met, potentially eligible survivors will be sent a letter of approach from their transplant center describing the study, and requesting permission to provide their contact information to NMDP/Fred Hutch. The letter will include a response form, stamped return envelope, study email address, internet URL for the study, temporary participant study ID code and toll-free phone number for survivors to contact NMDP/Fred Hutch to discuss the study or to contact the transplant center Study Coordinator or PI. NMDP will be the default contact for survivors through the study toll-free line, but contacts may be escalated to Fred Hutch as needed based on survivors' questions or concerns about study participation. Initial letter contact will be followed with three phone calls and then one more letter to those who do not respond with a total of up to six phone calls until the participant is reached and indicates interest or declines to participate. Up to three voice messages will be left. After participants return the response form to the consortium sites agreeing that their contact information can be given to NMDP/Fred Hutch study staff, or participants log onto the study internet site and consent, or they contact the Study Coordinators directly by phone or email, all further study activities will be handled by the NMDP and the Coordinating Center. The exception is if survivors from the consortium sites have medical questions. As agreed by the consortium PIs, such questions will be directed by a study investigator at Fred Hutch to the PI at the participant's transplant center.

Enrollment will continue until targeted goals are met, as defined for each targeted outcome in Table 3. We expect this to require 492 participants enrolled in the randomized study.

Consent

Before accessing the study questionnaires or any of the secure internet content, the electronic consent form must be agreed to and submitted. Consent will be indicated to include: 1) communication by email and phone (required), access to the secured online internet site (required), and social media (optional), 2) response to self-report assessments, and 3) allowing study access to medical records. After consenting, survivors will be registered for the study with the Fred Hutch study registration office.

Consent, with HIPAA content, will be electronically signed online. Survivors will be able to review and print the consent document before consenting via the online site, as they desire. If survivors have questions or concerns before signing the consent, we encourage them to contact us by phone or by email (inspire@fredhutch.org). Consent will be obtained using forms approved by the Institutional Review Board of Fred Hutch.

Consenting Information about Treatment Conditions. Survivors will be told that the research focus is on decreasing distress and increasing health care understanding and actions for people 2 to 5 years after transplant. They will be told that there are two possible groups: 1) full INSPIRE online program and study materials access, with mailed treatment summary and survivorship care plan (TS-SCP) for the survivor and, if they choose to provide names, for their health care providers, with an optional orientation call at 2 weeks and optional self-management calls at 6 weeks; or 2) access to a study website with links to other online resources for survivors, with delayed INSPIRE program access after completion of the 12-month assessment. They will be advised that they will be contacted if we detect severe emotional needs during the course of the study.

The first 100 participants who are approached, with an expected N=20 enrolled for the randomized study, will be treated as "run in" participants to test the website programming and study intervention procedures.

They will be approached and treated as regular participants from survey to data management randomization and intervention. These participants will receive the same access and study experience as later participants, but they will not be included in the outcome analyses or the N=492 sample size. Thus the total enrollment is projected to be N=512.

Response to Elevated Depression Scores at Baseline or Later Assessments

After baseline assessment, responses on the primary outcomes will be scored to determine whether the participant meets eligibility criteria for randomization and whether a suicide and depression screening trained study investigator needs to contact the participant for concerns about major depression. At least weekly, the Project Manager will review baseline assessments. She will bring any severe depression or other concerns to the attention of Drs. Yi, Syrjala, Baker or Majhail. Of note, the depression measure, PHQ-8, does not include a question about suicidal thoughts.

If possible major depression or risk to the survivors' health in other ways is detected, we have planned standard, IRB approved procedures With a score of 20 or greater reported on the PHQ-8 depression measure, a study investigator trained in depression and suicide screening will attempt to contact the survivor to by phone to screen for suicide risk, and encourage them to discuss their symptoms with their home medical provider. The study investigator will leave 3 phone messages over 2 weeks with a phone number to contact the study investigator. The study investigator may also send an email message, without PHI or indication of the reason for the call. All email or voice mail will indicate only that the study investigator is contacting the participant about his/her participation in the study, and will ask the participant to contact the study investigator. If there is no contact with or response from the participant after 3 attempts over 2 weeks, the study investigator will mail a letter to the participant stating that the study team is attempting to contact the participant, and providing the study toll-free phone number and email address, after which no further attempts to reach the person will be made. Once a participant is reached, the study investigator `will complete the safety evaluation which will include: 1) the nature of the suicidal thoughts or severe depression, 2) any suicide plan, 3) risk factors for suicide, 4) family, close friends or health care providers who are aware of or treating the participant's depression and/or suicidal thoughts or plans, and 5) overall risk for suicide and safety of the participant. If safety concerns remain, the study investigator may contact 911 or a family member to take the participant to an emergency room for evaluation, or follow other requirements indicated by state law (e.g., calling the county designated mental health professional [CDMHP] to evaluate the participant for potential involuntary psychiatric hospitalization). If safety is not judged to be an immediate risk, the study investigator and participant will review available local resources and make a plan for addressing severe depression or suicidal thoughts. The study investigator will encourage the participant to discuss thoughts and symptoms with his/her health care provider as appropriate. If needed, the study investigator may follow-up with an additional call to assure participant safety and use of available resources. A call record, with written risk assessment information, will be stored in a locked file separate from other study data. The form used for this depression and suicide screening is in the attachments. The study investigator will inform a study PI about the safety evaluation within 72 hours after ensuring the safety of the participant. The PI will decide if an adverse event has occurred. This contact will also occur if any participant receives a score of 20 or greater on the depression measure (indicating severe depression) at 3 or 12 month outcomes. These survivors will remain eligible for study randomization. In our previous internet studies, <1% indicated severe depression requiring a phone call.

Stratification and Randomization

Those who complete the baseline assessment but are determined to be ineligible after baseline assessment will be given access to the online INSPIRE site as a courtesy. Those who meet all eligibility criteria will be randomized based on the stratification criteria described below. If any one of the following scores on baseline patient reported outcomes (PRO) is impaired, the participant will be randomized within 'Group 1,' if no scores are impaired the participant will be randomized within 'Group 0' for the primary and secondary endpoints: a) Cancer and Treatment Distress (CTXD score <0.9 vs. ≥0.9), b) cardiometabolic health care adherence (<80% vs.≥80%) and c) cancer health care adherence (<80% vs.≥80%). Note that each of these endpoints of the study has a measure cut-point for eligibility for Group 1 randomization required at baseline, and these are the threestratification parameters below. However, all eligible participants will be randomized

as they will all contribute data for secondary analyses. After minimum required baseline assessment is complete and eligibility confirmed, the Project Manager will fax the registration office with stratification data for randomization. Stratification factors are based on whether the participant exceeded or fell below the cut-offs for these endpoints, as determined by baseline screening values, prior to randomization. We will not stratify on age, sex, cGVHD treatment, or race/ethnicity because we believe these will be balanced adequately between study arms through random selection, and we will adjust, or stratify on these factors as needed in analyses. Participants in both groups will then be randomly assigned to either the "Control" or "Intervention" arms. The PIs and Biostatistician will review participation rates within each stratum annually and adjust the algorithm if needed. Once enrollment is complete, the sampling probability relevant to each participant will be stored in the database for use in analyses. Randomization assignment of the participant will be communicated to the participant through email. A diagram of study randomization is shown in Figure 2 and will occur as follows.

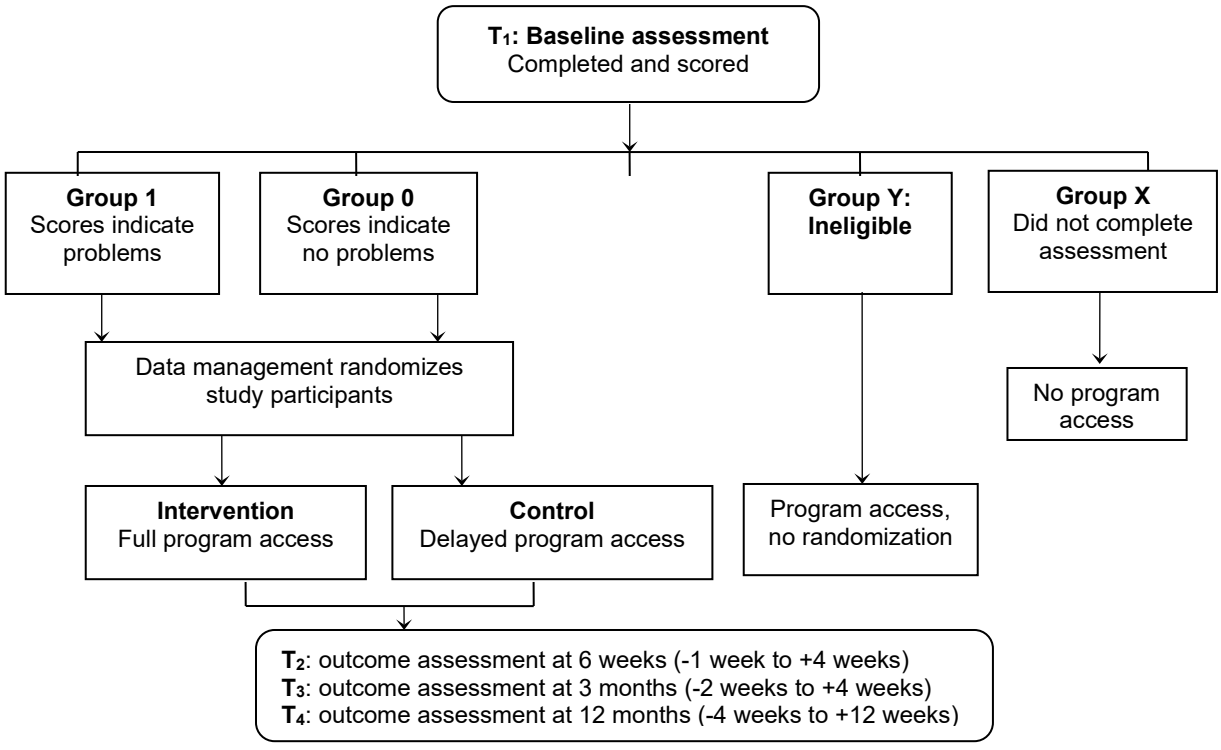
Group 1. Meets all eligiblity and has one or more elevated distress or low cardiometabolic or cancer health care adherence and is randomized to one of the two groups, intervention or control.

Group 0. Meets all eligiblity and does <u>not</u> have elevated elevated distress or low cardiometabolic or cancer health care adherence and is randomized to one of the two groups as in Group 1.

Group Y. Does not meet eligibility criteria (in active cancer treatment in the past 2 years, transplanted for disease other than hematologic malignancy or myelodysplasia, more than 5 years after first or last transplant.) Not randomized, but if consents and completes assessments (which determine final eligibility criteria) is given access to the INSPIRE online program but does not receive mailed TS-SCP, phone calls, or the follow-up assessments at 1, 3, and 12 months. .

Group X. Not randomized; consented but did not complete baseline assessment; is not given access to the INSPIRE online program but still registered with Data Management.

Figure 2. Diagram of randomization and treatment intervention possibilities.



Blinding

To reduce potential for contamination of the treatment and control conditions, the site investigators and NMDP study coordinators who contact survivors to respond to study questions or for incomplete assessments will be blinded to randomization. Information on randomization will be kept separate from the other data in a protected file viewable only to investigators and study staff who have intervention contacts with participants.

Participant Randomization Notification

To maintain randomization blinding of NDMP study coordinators completing the study assessment contacts with participants and study status tracking, the Project Manager will email survivors their randomization with internet site link and contact reminders for questions. She will give all participants the options to call the study toll-free line or the Coordinating Center with any questions.

Treatment

Intervention: Full Internet Program Access

Treatment Internet Site and Related Materials. The INSPIRE internet site will be continuously available to the participant for the study year. It will consist of the following six levels: 1) A greeting home page, with links to each target area. 2) Lift Mood, emphasizing managing stress and emotions. 3) Boost Heart Health pages focusing on implementation of the SCP addressing overall health behavior recommendations with a focus on cardiometabolic health. 4) Prevent Cancer pages focusing on implementation of the SCP for cancer screening tests and behaviors that prevent cancer. 5) Getting Connected, focusing on social activation and using resources to improve mood. 6) Tips and Tools, with downloadable content and tracking worksheets for monitoring progress on goals. There will also be options for participants to send secure messages with questions or comments on any topic to the study and links to the study Facebook page maintained and monitored by the study staff. The secure Facebook page will offer notices and encourage return to the site. Twitter and Instagram will have the same messages. We will increase motivation by email 'pushes', and mobile application notifications to cue survivors to links that match needs, and encourage use and tracking of the SCP. After completing the 12-month assessment, participants will receive a $25 gift card from Amazon, to be mailed to them as study payment.

Tailoring will include: 1) use of the participant's first name on logins, 2) recommended links to site landing pages specific to the participants' baseline elevated scores, 3) participants will receive tailored 'push' email links at 8 times after randomization, and 4) participants will receive mailed individualized TS-SCP with information about their cancer treatment and current recommended preventative health care guidelines. Health care providers listed on the baseline assessment will be sent as TS-SCP with an abbreviated listing of the recommended SCP screening and a focus on cardiometabolic health and cancer screening.

Stepped Care Self-Management Telehealth Contacts. Group 1 intervention participants who at the T2 (6 weeks) indicate no use of the online program, or lack knowledge of their cardiometabolic or subsequent malignancy risks, or do not indicate improvement in distress, will receive telehealth contacts. These will be three to four calls via phone. Calls will last 20-30 minutes for the first call and 10-20 minutes for the 'booster' calls. They will be led by a 'coach' trained by the clinical investigators in HCT and self-management skills, using a manual to deliver call content focused on assisting survivors with using the self-management skills in the online program. This is a brief, manualized intervention is designed to be sustainable without extensive clinical training and has been tested. The first session will focus on impairments indicated by the T2 6-week screening PRO. The coach and participant will make shared decisions, led by the participant, on goals and an action plan for addressing deficits, and elicit potential barriers and their solutions based on chronic disease self-management models (Figure 1).[1, 84, 133, 140-143] The second and third 'booster' calls will review progress on the action plan, address barriers and agree on a revised plan if needed. Participants and coaches will decide whether a fourth call would be helpful based on the complexity and difficulty of the goals and action plans. The contacts will be audiotaped for process evaluation

of content and fidelity to the self-management script.

Control: Website with Links and Delayed Internet Program Access

Participants randomized to receive the website providing links to existing transplant and cancer survivor sites and delayed access to the INSPIRE internet program (control) arm will be notified that they will be able to access the secured internet content after one year, and in the meantime will be provided with links to existing online resources and survivor sites. They can access the study content after they have completed their 12-month outcome assessments. At that time, the Project Manager will have their web permissions modified so that all internet study content can be accessed until the study closes. Internet site access will be as described above in 7.5.1. Control participants will also receive mailed individualized TS-SCP at randomization. After completing the 12-month assessment, control participants will also receive a $25 gift card from Amazon, to be mailed to them as study payment.

Group Y Website Access

Survivors who do not meet inclusion criteria will be ineligible for randomization. These survivors will, however, have full access to the internet site if they have completed the required baseline assessment. But they will not receive the mailed TS-SCP or the follow-up assessments at 1, 3, and 12 months.

Group X

Survivors who have consented to participate but not completed the baseline assessment cannot be randomized and cannot access the study internet content at any point.

8.0 EVALUATION

Table 1. PRO Measures and schedule of administration (T2 for intervention-only participants described in section 8.1)

8.1 Patient Reported Outcome Measures	T1 Baseline Screening	T3 3 month Outcome	T4 12 month Outcome
Primary Outcomes			
Cancer and Treatment Distress (CTXD)	X	X	X
Health Care Adherence (HCA)	X		X
Secondary Outcomes			
Patient Health Questionnaire-8 Depression (PHQ8)	X	X	X
Moderators and Risk Factors			
Computer and Mobile Phone Use	X		
Background: potential barriers to PCA (age, income, rural/urban, gender, cancer and treatment history, current medical history, medications)	X		
GVHD Symptom Scale (allogeneic only)	X		
Medical Comorbidities and Medications	X		X
Mediators			
Knowledge of Survivorship Needs	X	X	X
Health Self-Efficacy	X	X	X
Study Evaluation			
Evaluation of Program and Participation			X
ESTIMATED TIME REQUIRED	30-40	10-15	25-35

Measurement Selection Rationale

Study measures have all proven sensitive and specific in our research with HCT survivors, except Knowledge of Survivorship Needs which is in testing. Most are standardized measures with population norms. Measures were selected to target outcomes or as descriptive variables or mediators or moderators of outcomes as defined by the aims.

Measurement Time Points

The measures and their administration time points for three of the four assessments are listed in Table 1: baseline, 3 and 12 months. For group 1 intervention participants only, there will also be a brief orientation call for the study at 2 weeks, and an assessment at 6 weeks, that determines distress and knowledge of survivor health risks. Distress is measured on a 0-10 distress thermometer rating scale (0=no distress, 10=extreme distress) is >5, along with the first 2 items on the PHQ scored <=2 indicating low distress and depression symptoms. The distress thermometer is a widely used, validated and reliable measure of distress in cancer survivors.[144-147] Knowledge of HCT Survivor Health Risks is an 11-item screening for cardiometabolic and subsequent malignancy risks. Items are scored 0 ('my risk is higher') or 1 ('my risk is not different' or 'not sure') with a score >2 indicating inadequate knowledge of risks and eligibility for telehealth stepped care. The third criterion is whether the participant has viewed at least 3 pages of the online INSPIRE site. If any one of these 3 progress criteria are not met, intervention participants are stepped into telehealth self-management contact as described in Treatment section 7.5.1.

Baseline and Outcome Assessments

After consent, survivors will be directed to the 30-40 minute online baseline assessment. Measures are listed in Table 1. They will have the option to return to the assessment, if it has not been completed. This process will be repeated at 3 and 12-month outcome assessments. If the assessment is not completed, the NMDP study coordinators will contact the participant by phone and determine whether the assessment can be completed on the internet, if not, whether the assessment can be completed by mail.

Patient Reported Outcomes (PRO)

Primary Outcomes

Cancer and Treatment Distress (CTXD). The CTXD is a 22-item inventory of distress or worry related to stressful events for cancer survivors.[25] The measure was developed by the PI from structured interviews with HCT patients, nurses and physicians and has been tested with long-term survivors (N=1978). Testing supports its value as a predictor of health outcomes and it has been used in several RCTs.[6, 148-150] Internal reliability for HCT survivors is α = .93. There are 6 reliable subscales: uncertainty, health burden, family strain, finances, medical demands, identity.[151]

Health Care Adherence (HCA). The HCA is derived from the Cornell Service Index.[152] We have tested the format with several thousand HCT survivors.[153] Scores are transformed to proportion of HCA recommendations met. For a primary outcome, we use HCA items reflecting adherence to cardiometabolic surveillance (HCA-cardio; 5 items). Additional items measure adherence to subsequent malignancy surveillance (HCA-cancer; 7 items) and will be a secondary endpoint (see below). Items are adjusted for sex and age at which tests are recommended. An item is scored as 'adhered to' if the participant is under the age of recommended test onset. Cut point for determining adherence for each item is based on the frequency of testing recommended in guidelines (annual, every 3 or 5 years). Score is calculated as percentage of tests completed. Since adherence is important to reduce mortality risk, we set the cutoff for not meeting adherence criteria at <80%. In our previous 6-site INSPIRE study, we found 34% not adherent to HCA-cardio surveillance using the above criteria. Validity for HCA-cardio is supported by the following associations (p<.01 for all):

HCA-cardio was higher in those with self-reported high blood pressure, diabetes, history of heart attack, and those told they had cardiomyopathy or atherosclerosis. Discriminant validity is supported by no significant association of HCA-cardio with report of a history of second cancers, osteoporosis, or thyroid problems. The 21 Barriers to HCA items were defined from qualitative patient reports of HCT survivors.[154] With 6 subscales, the overall and subscale reliabilities are all α > 0.80. Mean score with cut point >0.45 will be used as an Aim 2 predictor. with subscales: Cost, Avoidance, Time, Knowledge, Provider Access, .

Secondary Outcomes

Patient Health Questionnaire (PHQ-8). The 8 item PHQ8 scale is highly reliable, valid and widely utilized in medical and psychiatric studies.[155-157] We have extensive data documenting reliability and utility in survivors.

Health Care Adherence for subsequent malignancies. As described above, our assessment of HCA includes 7 items measuring adherence to surveillance for subsequent malignancies. Scoring will be carried out as described for the primary HCA-cardio outcome and will use a cutoff for not meeting adherence criteria at <80%. In our previous 6-site INSPIRE study, we found 45% not adherent to HCA-cancer surveillance using the above criteria. Validity for HCA-cancer is supported by a marginal association with history of second cancer, with a 17% cumulative incidence rate in study participants (62% adherent vs. 54% occurrence rate for second cancers in the early post-HCT period; p =.074).

Moderators for Primary Outcomes and Risk Factors for Secondary Analyses

Background. Standard questions will define demographic characteristics including age, income, rural/urban by zip code, gender, ethnicity, education, work status, current medications, and cancer history.
Comorbidity Index and General Health. The self-report comorbidity index has strong kappa agreement with the Charlson comorbidity index, which is scored from medical records. Studies document the accuracy of HCT survivor self-report of medical diseases and problems when compared with medical records.[165][166] Medications will also be reported. It has documented validity and test-retest reliability, and used in our previous studies.[165-167]
GVHD Symptom Scale. For allogeneic HCT recipients, a reliable, validated measure based on cGVHD severity; type and duration of medications for cGVHD.[168]

Mediators for Primary Outcomes

Knowledge of Health Care Needs. This 15-item measure addresses 2 factors: 1) knowledge of treatment and related risks, including cardiometabolic and second cancer risks, and 2) understanding of health care recommendations and emotional health resources after HCT as included in our intervention. With N=936 participants in our previous INSPIRE study, alpha is strong for the overall score (α = .92) and factors (α = .82, (α = .93). The measure is derived from a similar measure developed in our SCOEN collaborations.[82]
Health Related Self-Efficacy. This measure reflects beliefs about health-related self-efficacy.[169, 170] In testing with N=860 HCT survivors, the measure has reliability of α = 0.86.

Process measures

These measures will provide intervention engagement, fidelity, and descriptive data. After intent to treat analyses, they will provide covariates for analyzing differential efficacy of the intervention.

Reach: rates of participants approached vs. registering, by age, urban/rural, ethnicity, and race diversity criteria. Engagement based on: Adoption: rates of visit to the site at least once and view at least 3 pages. Pages Viewed: number of logins and pages viewed per participant, and which pages viewed within content areas. Modalities Used: rates and characteristics of those using the internet site, social media, and requiring telehealth contact. Attrition: rates of request to withdraw or non-response to requests to complete assessments. Support Requests: rates and types of calls, emails, and comments (technical help vs. content of website questions or comments). Study Evaluation. Participants will report on use of the SCP, whether they took it to their providers and/or discussed it, use of the internet site, satisfaction, helpfulness and suggestions. Telehealth Contacts Fidelity, Engagement, and Extent participant completed action plan, and audiotape fidelity ratings by Dr. Baker and Yi for a minimum of 20% of sessions per coach interventionist.

Cost and Resource Tracking

We will track the costs of maintaining the program if disseminated (not including elements required for research implementation) as indicated by 1) materials, 2) programming for site maintenance, technical problem solving, and updating content and maintaining social networking, 3) multi-center staff time for identifying, approaching and tracking participants, and responding to participant comments 4) coordinating center and CIBMTR/NMDP staff time for tracking participants, responding to participant comments and requests, and responding to technical problems. We will track costs separately for the self-management call component. Site staff will report cost summaries quarterly. These will be standardized to report the cost per participant who reaches at least one of the primary endpoints for the study, specified for each type of cost (materials, staff time) as well as total costs. Because we will track the costs of preparing SCPs and internet links provided to the control group and will know their outcomes, we will also be able to calculate an incremental cost-effectiveness ratio for the internet intervention program compared to the control cost-effectiveness, similar to the method described by Mandelblatt and colleagues.[171, 172]

Medical Records

For cohort description and covariates, diagnoses and treatment-related variables will be downloaded or abstracted from the participating transplant center medical records.

Internet data security

The study internet site from the previous INSPIRE research project underwent review with and met specifications from the Information Security Office at Fred Hutch in July 2019. Fred Hutch developed a secured patient portal, to secure the identities of participants and their data. To protect the privacy of patient data, once participants 'submit' their assessment responses or two weeks go by without activity, assessments completed are permanently secured behind a firewall and cannot be accessed again. The same site and portal will be used in the current project, with updated content.

9.0 DRUGS, IRRADIATION AND MARROW/STEM CELL ADMINISTRATION TOXICITIES AND COMPLICATIONS

Not applicable.

10.0 GUIDELINES FOR ADVERSE EVENT REPORTING

Adverse Event Reporting/Institutional Policy

The following guidelines are the minimum Cancer Consortium IRB adverse event (AE) reporting guidelines. Protocol-specific additional reporting requirements for adverse events are addressed in Section 10.2. In

accordance with institutional policy, all adverse events which in the opinion of the principal investigator are unexpected and related or possibly related to the research and serious or suggest that the research places research participants or others at greater risk of physical or psychological harm than was previously known or recognized be reported to the IRB within 10 calendar days of learning of the problem.
Institutional support of trial monitoring will be in accordance with the Fred Hutch/University of Washington Cancer Consortium Institutional Data and Safety Monitoring Plan. Under the provisions of this plan, Fred Hutch Clinical Research Support coordinates data and compliance monitoring conducted by consultants, contract research organizations, or Fred Hutch employees unaffiliated with the conduct of the study. Independent monitoring visits occur at specified intervals determined by the assessed risk level of the study and the findings of previous visits per the institutional DSMP. Independent monitoring meetings occur annually or more often as determined by the findings of the previous meetings (see DSMB charter.)

Definitions:

Adverse Event - Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product, medical treatment or procedure and which does not necessarily have to have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, medical treatment or procedure whether or not considered related to the medicinal product.

Life-threatening Adverse Event – Any adverse event that places the patient or subject, in view of the investigator, at immediate risk of death from the reaction.

Unexpected Adverse Event – An adverse event is “unexpected” when its nature (specificity), severity, or frequency are not consistent with (a) the known or foreseeable risk of adverse events associated with the research procedures described in the Protocol-related documents, such as the IRB-approved research protocol, informed consent document and other relevant sources of information such as product labeling and package inserts; and are also not consistent with (b) the characteristics of the subject population being studied including the expected natural progression of any underlying disease, disorder or condition any predisposing risk factor profile for the adverse event.

Serious Adverse Event (SAE) – Any adverse event occurring that results in any of the following outcomes:

- death
- a life-threatening adverse event (real risk of dying)
- inpatient hospitalization or prolongation of existing hospitalization
- a persistent or significant disability/incapacity
- a congenital anomaly
- requires intervention to prevent permanent impairment of damage

Attribution - The following are definitions for determining whether an adverse event is related to a medical product, treatment or procedure:

- An adverse event is “**related or possibly related to the research procedures** “if in the opinion of the principal investigator, it was more likely than not caused by the research procedures.
- Adverse events that are solely caused by an underlying disease, disorder or condition of the subject or by other circumstances unrelated to either the research or any underlying disease, disorder or condition of the subject are not “related or possibly related.”
- If there is any question whether or not an adverse event is related or possibly related, the adverse event should be reported.

The Cancer Consortium Expedited Reporting Form should be completed for all adverse events that meet the expedited reporting requirements. The AE form should be faxed to the IRO at (206) 667-6831. All available information should be submitted.

Study-Specific Adverse Event Capture and Data Safety and Monitoring Plan

Based on previous similar research with internet-based behavioral treatment conducted with survivors who have recovered from acute treatment effects and are living independently, this study is not expected to have Serious Adverse Events (SAE). We will contact and collect data from participants at baseline, 6-weeks, 3 months and 12 months. We plan ongoing recording of adverse events for each participant, each reviewed by the PI within 7 days. Any SAE will be immediately reported to the PI and the IRB according to requirements in the standard Fred Hutch DSMP. As Coordinating Center, Fred Hutch will complete the Fred Hutch/UW Cancer Consortium Expedited Reporting Form for all adverse events, including those associated with participants enrolled from the participating consortium centers. Ad hoc meetings will be called by the PI for any SAE, for two similar Adverse Events, or at any time by any other study staff or investigator for a data or participant safety concern. A physician member of the research project will provide the medical monitoring for all adverse events. Adverse events and SAE will be reviewed annually by the Fred Hutch standing Data Safety and Monitoring Board and Institutional Review Board in addition to the immediate reviews for SAE just described.

The Study Coordinator continually monitors patient report data and prepares weekly updates of project activity for the investigators. Risks related to the study that are expected or seen previously in similar studies include increased distress, complaints that the study material makes the participant feel worse by reminding him or her of problems, or complaints that assessments are too long. Immediate contact is made with a participant and psychological support is available if any complaints are received. Historically, with the prior internet sites implemented with N =1336 participants for R01 CA112631 and with N=1087 participants for R01 CA160684, none of these events have been serious and all have been resolved immediately with discussion or withdrawing the participant from the study. Serious adverse events which could possibly be related to the study include: a) complaints of intrusiveness or violation of privacy from the study (not just choosing to drop out of the study), b) anger, threats of harm or legal action against the study or a person, c) hospitalization for depression or anxiety, or d) physical harm as a result of a participant's health care provider following the screening guidelines and ordering a test that causes the participant harm.

The following steps will occur in documenting adverse events for this study:

1. For any adverse event that is *Serious, Unexpected*, *and Possibly Related* to the study, the Investigator, or other study personnel who first becomes aware of the event will complete the Adverse Event form and will fax it to the PI, Dr. Baker within 48 hours. FAX: 206-667-4356 (confidential secure fax). If Dr. Baker is unavailable, Dr. Jean Yi, as Project Director, will perform her activities.
2. The PI together with the investigator(s) who observed or reported the adverse event will assess causal relationship between the study procedures and the adverse event. They will also assess severity at this time. This will be done within 48 hours after notification of Serious Adverse Events, and within 7 days for all other adverse events.
   At this time, the PI will define a ***Response Plan*** for follow-up of the adverse event, determining:
   0 = No further response to the participant is needed.
   1 = Investigator told of event should follow-up to assure event has been adequately treated.
   2 = Further recommendations need to be offered to the participant and who will follow-up to provide these recommendations.
   3 = Additional treatment is needed, treatment recommendations are defined and an Investigator is designated to facilitate finding treatment if the participant is willing.
   4 = If participant or other person's safety is in question, the PI/Project Director will determine whether a treating physician needs to be contacted to maintain safety. If so, an Investigator will be designated to make that contact and to follow-up to determine the outcome.
   A notation will be made as to whether the adverse event resulted in the patient terminating the study.
3. The PI or Project Director will complete an SAE form and fax it to the Fred Hutch DSMB and IRB within 48 hours of receipt of the form and within 7 days of when the event becomes known.
4. Within 7 days of any non-serious adverse event during the study, the Investigator or study personnel observing or first being told of the event will fill out this form and fax it to the Project Director.

5. At each weekly team meeting, a regular agenda item will be to review Adverse Events. Documentation of no events or the nature of events will be included in team meeting minutes. Adverse Event forms will be sent to all site PIs and their Study Coordinators for their use, although we do not expect AEs from contacting the survivors for participation. Adverse Event forms will be retained, tallied and reported annually to appropriate agencies by the Study Coordinator.
6. All Adverse Event Forms and SAE will be reviewed annually by the Fred Hutch standing DSMB. At this time, they will prepare an adverse events summary to send to all Investigators and in annual reports. To reduce the likelihood of a similar occurrence the PI will schedule further discussion between staff if an adverse event is related to the study and is grade 2 or higher. This plan, as well as a summary of adverse events and copies of the SAE forms completed since the last renewal, will be reported to the DSMB, IRO and NCI program officer annually. Forms will then be filed with the patient's confidential data, without identifiers.

11.0 DATA CONFIDENTIALITY

Only code numbers will be used on data. Only staff who have been trained in human subjects protection and have signed confidentiality statements will have access to study information. All hard copy data is stored in locked file cabinets in locked offices. All data will be locked and password or keycard protected at all times. All computerized data files will be password protected with passwords requiring regular updating. All clinical computing internet-related electronic data will be maintained on a secure web fileserver with backup and protection against unauthorized access, as with other computer databases. Access to the database and programs will be controlled through requirements for unique accounts and passwords. Passwords will have a limited expiration life and will need to be reset quarterly for continued use. The contents of the secure web server including program source code, web site information and data will be written to backup media daily. Additionally, the study will have a secure online site, using the Clinical Oncology Research Entrance (CORE), for file and data sharing with Clinical Data Systems and Clinical Research Data Systems and across transplant centers.

The Clinical Data Systems department will provide server security. All electronic data will be maintained on a secure internet fileserver with backup and protection against unauthorized access. Access to the database and programs will be controlled through requirements for unique accounts and passwords. The contents of the secure internet server including program source code, internet site information and data will be written to backup media daily. All hard copy data will be stored in locked file cabinets in locked offices, without personal identifiers.

12.0 STATISTICAL CONSIDERATIONS AND DATA MANAGEMENT

Projected Target Accrual for Randomized Study
ETHNIC AND GENDER DISTRIBUTION CHART

Table 2. Anticipated/Planned Enrollment for Entire Randomized Study* Number of Participants (*must provide exact numbers. i.e. no range)*				**Non-Randomized Participants***
Ethnic Categories	**Sex/Gender**			
	Females	Males	Total	Total
Hispanic or Latino	15	15	30	6
Not Hispanic or Latino	242	240	482	144
Ethnic Categories: Total of All Participants*	257	255	512	150
Racial Categories				
American Indian/Alaska Native	3	2	5	3

Asian	6	6	12	2
Native Hawaiian or Other Pacific Islander	2	2	4	0
Black or African American	16	10	26	11
White	230	235	465	134
Racial Categories: Total of All Participants *	257	255	**512**	**150**

Design

Enrollment. We expect to approach 1358 potentially eligible survivors who are between 2-5 years after HCT. Of these, 100 will be run-in approaches with a projected 20 enrolled and randomized, but not included in analyses. We project enrolling an additional N=492 eligible for a two-arm randomization to reach the sample sizes needed for each of the two primary endpoints. An additional projected 100 are expected to register and consent for the study, but either not complete baseline assessment required for randomization or to not be eligible for randomization after baseline assessment because of treatment in the past two years or other exclusion criteria. They will be given access to the INSPIRE site as a courtesy. We expect another group of 50 participants will consent but will not be eligible for randomization due to incomplete baseline assessment. *Randomization*. Those with one or more targeted complications will be randomized to one of 2 arms (Group 1). Those without targeted complications will be separately randomized to one of 2 arms (Group 0). We expect approximately 305 will be eligible for Group 1 randomization and inclusion in one or more of the analyses of the 2 primary outcomes. To have sufficient power for each of the two primary endpoints, we will need to enroll 197 participants for the elevated distress outcome and 239 for the cardiometabolic non-adherence. Participants who do not qualify for analysis of either primary endpoint (Group 0) will be important for inclusion in secondary analyses and will also be randomized to intervention vs. control arms. Based on our experience in the previous internet grant, we project a loss of about 28% in the course of the study implementation from consent to 12-month assessment, 8% from mortality or severe medical problems. With 305 participants randomized to Group 1 for the primary analyses, this provides sufficient power for aims 1, 2, 3 and secondary analyses.

Data Management

We anticipate limited missing data and out of range responses by using the internet-based assessment, with phone calls to check with non-responders and mailed short-forms completed if necessary, as was the case in our previous research. We have established a minimum, abbreviated set of forms that provide primary and secondary outcomes (CTXD, HCA, PHQ-8). Assessment programming will set parameters for allowable responses and will return responders to items either missed or outside range, with an option to click a ‘choose not to respond’ box. Validity checks will also be programmed to flag responses that are markedly inconsistent and may be invalid. Outliers will be identified and sent to the Dr. Yi and the mPIs to determine whether clinical response is needed. The mPIs will be notified and will contact a participant if validity seems questionable. They will assure that the participant personally completed the items and is cognitively capable of responding. In the past this has occurred only rarely, less than 1% of the time. A second level of flagging will occur when depression responses indicate severe depression, as we expect 2% of assessments. In these cases, the Project Manager will notify Dr. Yi. The Project Manager’s data will be coded without names and Dr. Yi will decode these.

Programming will provide for calculation of summary scores and data will be routinely downloaded to a project database. The Statistician will examine distributions for normality (e.g., outliers, skewness) and conduct appropriate transformations or category coding if distributions are non-normal. When data cleanup is complete, all files will be merged into a project database. The project database and all data collection, analysis, and storage will be maintained at the Coordinating Center. No study data will be maintained at the consortium sites.

Endpoints

The primary endpoints to be evaluated for the above hypotheses are CTXD (distress) and HCA-cardio. The primary and secondary endpoints for the study will be defined as binary outcomes. Participants will qualify for analysis of a particular endpoint if they meet eligibility at their baseline response for that endpoint (CTXD ≥0.9 or HCA-cardio<80% [primary endpoints], or HCA-cancer <80% [secondary endpoint], PHQ-8 score ≥10). Some participants will contribute to both primary endpoint analyses, and others to none or one . Similar conditional analyses will be carried out for the secondary endpoints. Stepped-care telehealth will be introduced based on PRO assessed at 6-weeks, then short term outcomes will be assessed after 3 months and delayed or sustained effects will be assessed at 1 year.

Primary Hypothesis

Aim 1: Among HCT survivors with poor health care adherence to cardiometabolic or subsequent malignancy surveillance and/or elevated cancer-related distress, determine the impact of a patient-centered, self-management stepped care program compared to an active control group provided access to HCT survivorship best practices.
Hypothesis 1: Participants with elevated cancer-related distress or poor health care adherence who receive the stepped care program will report reduced distress, and improved health care adherence for cardiometabolic or subsequent malignancy surveillance at 12 months when compared to controls.

Secondary Hypotheses

Aim 2: Determine characteristics of intervention participants who require telehealth stepped care at 6-weeks.
Hypothesis 2: Characteristics of intervention arm participants at the 6-week interim assessment who require telehealth stepped care because they 1) do not meet criteria for adequate knowledge of cardiometabolic risks, or 2) do not report improved distress, or 3) have not logged in to the online program will include those with higher depression or distress scores at baseline, more health care barriers at baseline, age 70+ years, male sex, people of color, lower income and education.
Aim 3: Determine resources that would be needed to sustain the intervention as a national HCT survivorship program if implemented through the CIBMTR//NMDP.

Primary Endpoint Tests of the Specific Aims

Hypothesis 1

Participants with elevated cancer-related distress or poor health care adherence who receive the stepped care program will report reduced distress, and improved health care adherence for cardiometabolic surveillance at 12 months when compared to controls.

Power Calculations

As described in Table 3, we expect to enroll a total of 492 subjects in order to attain the 197 and 239 participants needed to meet eligibility criteria for Group 1 randomization and inclusion in the intervention vs. control arm analyses of the 2 primary outcomes: dichotomous CTXD and cardiac HCA outcomes, respectively (some will be eligible for more than one). Among these, we estimate that 71 and 86 per arm will be available for analyses after the 12-month evaluation, respectively. Assuming control arm rates of events similar to or higher than those observed in the preliminary data from the INSPIRE study, these numbers of participants will allow us to detect a minimum relative risk of success for the intervention arm vs. the control arm of 1.9for the CTXD and for the HCA-cardio endpoints, with 80% power and two-sided α=0.025 for each comparison (α=0.05/2 = 0.025 to conserve overall α=0.05). For evaluation of the continuous versions of the outcomes, we will have at least 80% power to detect a minimum effect size of 0.52, and 0.47 for the CTXD andHCA-cardio outcomes, respectively (α=0.025 for each).

Table 3. Sample size calculations for Aim 1 primary outcomes, 80% power

Analysis Plan for Hypothesis 1

	CTXD	HCA-Cardio	
Enroll/Consent/complete baseline	492	492	
T1: Eligible for specific endpoint	**197**	**239**	
3 mo. voluntary withdraw or mortality/illness (4%)	[8]	[10]	
3 mo. non-responders, able to respond at 12 mo. (15%)	[30 eligible for T4]	[36 eligible for T4]	
T3: 3 mo. completers (81%)	**160**	**194**	
T4: 12 mo. potential cohort	**189**	**229**	
12 mo. voluntary withdraw or mortality/illness (5% of T4)	[9]	[11]	
12 mo. non-responders (20% of T4)	[38]	[46]	
12 mo. completers (75% of T4, 72% of T1)	**142 [71/arm]**	**172 [86/arm]**	

The primary endpoints to be evaluated for hypothesis 1 are distress score (CTXD) and the proportion of HCA-cardio within the past 12 months as reported on the HCA and will be defined as binary outcomes. Participants will meet the primary endpoint for lack of distress if they score <0.9 on the CTXD. They will meet the HCA-cardio endpoint if their percent of recommended screenings obtained within the past 12 months is ≥80% . The number and pattern of missing variables will be summarized and assessed to understand potential biases. If attrition is greater than 10% before the 12-month follow-up, we plan to utilize multiple imputation of the primary outcome and to carry out sensitivity analyses of the impact of missing data on the comparisons between study arms.[173]
For Hypothesis 1, the two primary endpoints, evaluated at the 12-month time point among the subjects identified at baseline as impaired for that particular endpoint criteria will each be compared between study arms as intent to treat analyses using standard logistic regression analyses, adjusted for cancer center and utilizing a two-sided α=0.025 level of significance to preserve type I error at 0.05 overall for the two primary endpoints. If other factors appear to be imbalanced between study arms, we will adjust analyses for those factors. Secondary analyses will evaluate depression alone, a PHQ-8 score $\geq$10 (essentially a subset of those with distress) and HCA-cancer in a similar manner as carried out for the primary endpoints. Continuous versions of the tests comprising the primary and secondary endpoints using linear regression models as well as adjusting or stratifying on engagement with the intervention (viewing at least 3 pages of the online program or completing telehealth calls) will also be carried out. Assumptions regarding normality of the outcomes will be assessed, although examination of outcomes in preliminary data suggests this is a reasonable assumption, with no significant skew in the distributions. If assumptions are not met, appropriate transformations will be implemented or alternative methods explored (e.g. non-parametric methods).

Hypothesis 2

Characteristics of intervention arm participants at the 6-week interim assessment who require telehealth stepped care because they 1) do not meet criteria for adequate knowledge of subsequent malignancy and cardiometabolic risks, or 2) do not report improved distress, or 3) have not logged in to the online program will include those with higher depression or distress scores at baseline, more health care barriers at baseline, age 70+ years, male sex, people of color, lower income and education.

Analysis Plan for Hypothesis 2

Among subjects in Group 0 and Group 1 intervention arms, we will define the endpoint as a binary indicator of whether the individual required telehealth stepped care at the 6-week time point. We plan to use generalized linear models to evaluate associations between patient characteristic variables and likelihood of stepped care. Variables to be examined include age (<70 vs. 70+ years), sex, race/ethnicity (White non-Hispanic vs. Non-White or Hispanic, income (<$40,000 vs. $40,000 per year) and education (college graduate yes/no), PHQ8 depression >16, and Barriers to HCA > 0.45. The need for telehealth stepped care is not likely to be a rare event (rare being <10%) and thus odds ratios from a logistic regression model would not be good approximations of the relative risk (RR). Therefore, rather

than logistic regression we will likely use a log-link with Poisson error structure and robust sandwich variance estimates to directly estimate the more interpretable RR.[173] A multivariable model will be established using single-variable and step-up and step-down procedures with a liberal p-value for inclusion in the model ($p<0.2$). Factors identified as significantly ($p<0.05$) associated with the need for telehealth stepped care will be examined and based on the magnitude of the RR estimate and the prevalence of the particular patient characteristic, we will similarly examine indicators of response to the telehealth care based on continuous primary endpoints in that subgroup. This will establish a profile of types of survivors for whom modified approaches to care may be beneficial.

Aim 3 and Plan for Aim 3

Determine resources that would be needed to sustain the intervention as a national HCT survivorship program if implemented through the CIBMTR/NMDP.
This is a descriptive aim defining costs and resource requirements. Data relevant to resource utilization (costs) and methods of collection are described in section 8.3 Cost and Resource Tracking. All costs associated with the intervention and, separately, the control arms of the study for the Group 0 and Group 1 subjects in the study will be summed and standardized to per person costs. We will use these amounts to calculate an incremental cost ratio for the online intervention program and telehealth intervention component compared to the control cost, similar to the method described by Mandelblatt et al.[171, 172] The costs of maintaining the various components of the program, relative to their use, will be calculated separately for those in the Group 0 and 1 intervention arms, specific to maintaining the social media site, the internet program, and the telehealth calls (Group 1 only) relative to the number of participants using those components among intervention participants.

Secondary Analyses

Secondary endpoints will include depression, process measures describing internet study reach and utilization, as well as outcomes of knowledge of survivorship needs. We will compare secondary outcomes knowledge of health care needs between study arms using similar analytic methods as for the primary outcomes (both binary and continuous outcomes). We will also carry out subset analyses within stratum defined by the degree of utilization of the resources (i.e. more than one page viewed of internet site – see below for alternate definitions), and receipt of the phone calls if designated, to evaluate whether, among “users”, the tailored intervention has stronger effects.
Further analyses will identify risk factors for disparities in survivorship HCA in HCT survivors. Study reach, adoption and attrition process measures will be reported descriptively.
Primary analyses will be based on 12 month outcome measurements, but we will utilize the 3 month time point in secondary longitudinal analyses modeled after those carried out in DuHamel et al.[30] Additional secondary analyses will include evaluation of the impact of the internet intervention on continuous versions of the primary endpoints, but among all participants randomized, including those not meeting criteria for inclusion in primary analyses. This will provide estimates of the impact of study intervention on an unscreened population which would be a likely dissemination methodology.

12.9 Process Descriptive Analyses

Evaluation of the telehealth self-management calls will be based on 1) fidelity scored from audiotape reviews, 2) coach ratings, 3) completion rates of scheduled calls and 4) completion of action plans, and 5) barriers identified during calls. Additional descriptive analyses will be conducted on the process elements defined in section 8.4 Process Measures.

13.0 TERMINATION OF STUDY

Survivors in the intervention group will complete the intervention approximately 12 months after beginning (i.e., the date the patient received notification of randomization and website access). After completing the 12-month assessment, they will receive notification that they have completed participation in the study. Survivors will continue to have full access to the website after their official study participation has ended until the end of the study.

Survivors in the control (delayed internet site access) group will have full internet program access from the time they complete the 12-month assessment until the end of the study.

Survivors may withdraw from the study whenever they request to do so.

REFERENCES

1. McCorkle, R., et al., *Self-management: Enabling and empowering patients living with cancer as a chronic illness.* CA Cancer J Clin, 2011. 61(1): p. 50-62.
2. Syrjala, K.L., P.J. Martin, and S.J. Lee, *Delivering care to long-term adult survivors of hematopoietic cell transplantation.* Journal of Clinical Oncology, 2012. 30(30): p. 3746-3751.
3. Martin, P.J., et al., *Life expectancy in patients surviving more than 5 years after hematopoietic cell transplantation.* Journal of Clinical Oncology, 2010. 28(6): p. 1011-1016.
4. Ashton, L.J., et al., *A population-based cohort study of late mortality in adult autologous hematopoietic stem cell transplant recipients in Australia.* Biol Blood Marrow Transplant, 2014. 20(7): p. 937-45.
5. Sun, C.L., et al., *Burden of morbidity in 10+ year survivors of hematopoietic cell transplantation: report from the bone marrow transplantation survivor study.* Biol Blood Marrow Transplant, 2013. 19(7): p. 1073-80.
6. Syrjala, K.L., et al., *Recovery and long-term function after hematopoietic cell transplantation for leukemia or lymphoma.* JAMA, 2004. 291(19): p. 2335-43.
7. Mosher, C.E., et al., *Quality of life concerns and depression among hematopoietic stem cell transplant survivors.* Supportive Care in Cancer, 2011. 19(9): p. 1357-1365.
8. Andrykowski, M.A., et al., *Long-term health-related quality of life, growth, and spiritual well-being after hematopoietic stem-cell transplantation.* Journal of Clinical Oncology, 2005. 23(3): p. 599-608.
9. KL, S., et al., *INSPIRE: Structure and Implementation of an Internet Randomized Controlled Trial for Cancer Survivors Treated with Hematopoietic Stem Cell Transplantation.* Journal of Cancer Survivorship, 2010.
10. Syrjala, K.L., et al., *Efficacy of an internet randomized controlled trial for long-term cancer survivors after hematopoietic stem cell transplantation (HSCT).* Submitted.
11. Syrjala, K.L., et al. *Can an online program for survivors of hematopoeitic cell transplantation (HCT) imrprove access to resources? Reach results from INSPIRE, a multicenter randomized controlled trial (RCT)*. in *8th Biennial Cancer Survivorship Research Conference: Innovation in a Rapidly Changing Landscape*. 2016. Washington D.C.
12. Mosher, C.E., et al., *Physical, psychological, and social sequelae following hematopoietic stem cell transplantation: a review of the literature.* Psycho-Oncology, 2009. 18(2): p. 113-127.
13. Armenian, S.H., et al., *Long-term health-related outcomes in survivors of childhood cancer treated with HSCT versus conventional therapy: a report from the Bone Marrow Transplant Survivor Study (BMTSS) and Childhood Cancer Survivor Study (CCSS).* Blood, 2011. 118(5): p. 1413-20.
14. Hammond, C., J.R. Abrams, and K.L. Syrjala, *Fertility and risk factors for elevated infertility concern in 10-year hematopoietic cell transplant survivors and case-matched controls.* Journal of Clinical Oncology, 2007. 25(23): p. 3511-3517.
15. Duell, T., et al., *Health and functional status of long-term survivors of bone marrow transplantation.* Annals of Internal Medicine, 1997. 126(3): p. 184-192.
16. Chiodi, S., et al., *Quality of life in 244 recipients of allogeneic bone marrow transplantation.* British Journal of Haematology, 2000. 110(3): p. 614-619.
17. Socie, G., et al., *Busulfan plus cyclophosphamide compared with total-body irradiation plus cyclophosphamide before marrow transplantation for myeloid leukemia: long-term follow-up of 4 randomized studies.* Blood, 2001. 98(13): p. 3569-3574.
18. Braamse, A.M., et al., *Predictors of health-related quality of life in patients treated with auto- and allo-SCT for hematological malignancies.* Bone Marrow Transplantation, 2012. 47(6): p. 757-769.
19. Jim, H.S., et al., *Risk factors for depression and fatigue among survivors of hematopoietic cell transplantation.* Cancer, 2016.
20. Rusiewicz, A., et al., *Psychological distress in long-term survivors of hematopoietic stem cell transplantation.* Psychooncology, 2008. 17(4): p. 329-37.
21. Hefner, J., et al., *High prevalence of distress in patients after allogeneic hematopoietic SCT: fear of progression is associated with a younger age.* Bone Marrow Transplant, 2014. 49(4): p. 581-4.
22. Hamilton, J.G., et al., *Economic survivorship stress is associated with poor health-related quality of life among distressed survivors of hematopoietic stem cell transplantation.* Psycho-Oncology, 2013. 22(4): p. 911-921.
23. Stepanikova, I., et al., *Exploring long-term cancer survivors' experiences in the career and financial domains: Interviews with hematopoietic stem cell transplantation recipients.* J Psychosoc Oncol, 2016. 34(1-2): p. 2-27.
24. Pidala, J., C. Anasetti, and H. Jim, *Quality of life after allogeneic hematopoietic cell transplantation.* Blood, 2009. 114(1): p. 7-19.
25. Syrjala, K.L., J.C. Yi, and S.L. Langer, *Psychometric properties of the Cancer and Treatment Distress (CTXD) measure in hematopoietic cell transplantation patients.* Psychooncology, 2016. 25(5): p. 529-35.
26. Braamse, A.M., et al., *Distress, problems and supportive care needs of patients treated with auto- or allo-SCT.* Bone Marrow Transplant, 2014. 49(2): p. 292-8.

27. Artherholt, S.B., et al., *Risk factors for depression in patients undergoing hematopoietic cell transplantation.* Biology of Blood & Marrow Transplantation, 2014. 20(7): p. 946-950.
28. Loberiza, F.R., Jr., et al., *Association of depressive syndrome and early deaths among patients after stem-cell transplantation for malignant diseases.* Journal of Clinical Oncology, 2002. 20(8): p. 2118-2126.
29. Kenzik, K., et al., *Relationships among symptoms, psychosocial factors, and health-related quality of life in hematopoietic stem cell transplant survivors.* Support Care Cancer, 2015. 23(3): p. 797-807.
30. DuHamel, K.N., et al., *Randomized clinical trial of telephone-administered cognitive-behavioral therapy to reduce post-traumatic stress disorder and distress symptoms after hematopoietic stem-cell transplantation.* Journal of Clinical Oncology, 2010. 28(23): p. 3754-3761.
31. Bhatia, S., et al., *Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: report from the Bone Marrow Transplant Survivor Study.* Blood, 2007. 110(10): p. 3784-3792.
32. Majhail, N.S., et al., *Late effects in survivors of Hodgkin and non-Hodgkin lymphoma treated with autologous hematopoietic cell transplantation: a report from the bone marrow transplant survivor study.* Biology of Blood & Marrow Transplantation, 2007. 13(10): p. 1153-1159.
33. Baker, K.S., E. Chow, and J. Steinberger, *Metabolic syndrome and cardiovascular risk in survivors after hematopoietic cell transplantation.* Bone Marrow Transplant, 2012. 47(5): p. 619-25.
34. Majhail, N.S., et al., *Hypertension and diabetes mellitus in adult and pediatric survivors of allogeneic hematopoietic cell transplantation.* Biology of Blood & Marrow Transplantation, 2009. 15(9): p. 1100-1107.
35. Majhail, N.S., et al., *High prevalence of metabolic syndrome after allogeneic hematopoietic cell transplantation.* Bone Marrow Transplantation, 2009. 43(1): p. 49-54.
36. Abou-Mourad, Y.R., et al., *Long-term outcome after allo-SCT: close follow-up on a large cohort treated with myeloablative regimens.* Bone Marrow Transplant, 2010. 45(2): p. 295-302.
37. Baker, K.S., et al., *Diabetes, hypertension, and cardiovascular events in survivors of hematopoietic cell transplantation: a report from the bone marrow transplantation survivor study.* Blood, 2007. 109(4): p. 1765-1772.
38. Chow, E.J., et al., *Late Effects Surveillance Recommendations among Survivors of Childhood Hematopoietic Cell Transplantation: A Children's Oncology Group Report.* Biol Blood Marrow Transplant, 2016. 22(5): p. 782-95.
39. Saidi, A. and R. Alharethi, *Management of chemotherapy induced cardiomyopathy.* Curr Cardiol Rev, 2011. 7(4): p. 245-9.
40. Baker, K.S., S. Armenian, and S. Bhatia, *Long-term consequences of hematopoietic stem cell transplantation: current state of the science.* Biology of Blood & Marrow Transplantation, 2010. 16(1 Suppl): p. S90-S96.
41. Bhatia, S., *Long-term health impacts of hematopoietic stem cell transplantation inform recommendations for follow-up.* Expert Rev Hematol, 2011. 4(4): p. 437-52; quiz 453-4.
42. van Nimwegen, F.A., et al., *Cardiovascular disease after hodgkin lymphoma treatment: 40-year disease risk.* JAMA Intern Med, 2015. 175(6): p. 1007-17.
43. Armenian, S.H., et al., *Predictors of late cardiovascular complications in survivors of hematopoietic cell transplantation.* Biology of Blood & Marrow Transplantation, 2010. 16(8): p. 1138-1144.
44. DeFilipp, Z., et al., *Metabolic syndrome and cardiovascular disease following hematopoietic cell transplantation: screening and preventive practice recommendations from CIBMTR and EBMT.* Biol Blood Marrow Transplant, 2016.
45. Majhail, N.S., et al., *Secondary solid cancers after allogeneic hematopoietic cell transplantation using busulfan-cyclophosphamide conditioning.* Blood, 2011. 117(1): p. 316-322.
46. Bhatia, S., et al., *Malignant neoplasms following bone marrow transplantation.* Blood, 1996. 87(9): p. 3633-3639.
47. Curtis, R.E., et al., *Solid cancers after bone marrow transplantation.* New England Journal of Medicine, 1997. 336(13): p. 897-904.
48. Krishnan, A., et al., *Predictors of therapy-related leukemia and myelodysplasia following autologous transplantation for lymphoma: an assessment of risk factors.* Blood, 2000. 95(5): p. 1588-93.
49. Rizzo, J.D., et al., *Solid cancers after allogeneic hematopoietic cell transplantation.* Blood, 2009. 113(5): p. 1175-1183.
50. Friedman, D.L., et al., *Increased risk of breast cancer among survivors of allogeneic hematopoietic cell transplantation: a report from the FHCRC and the EBMT-Late Effect Working Party.* Blood, 2008. 111(2): p. 939-44.
51. Cohen, A., et al., *Risk for secondary thyroid carcinoma after hematopoietic stem-cell transplantation: an EBMT Late Effects Working Party Study.* Journal of Clinical Oncology, 2007. 25(17): p. 2449-2454.
52. Socie, G., K.S. Baker, and S. Bhatia, *Subsequent malignant neoplasms after hematopoietic cell transplantation.* Biol Blood Marrow Transplant, 2012. 18(1 Suppl): p. S139-50.
53. Baker, K.S., et al., *New malignancies after blood or marrow stem-cell transplantation in children and adults: incidence and risk factors.* J Clin Oncol, 2003. 21(7): p. 1352-8.
54. Inamoto, Y., et al., *Secondary solid cancer screening following hematopoietic cell transplantation.* Bone Marrow Transplant, 2015. 50(8): p. 1013-23.
55. *From Cancer Patient to Cancer Survivor: Lost in Transition. Improving Care and Quality of Life. Committee on Cancer Survivorship. National Cancer Policy Board.* 2010, Washington D.C.: National Academy of Sciences.

56. Ganz, P.A., J. Casillas, and E.E. Hahn, *Ensuring quality care for cancer survivors: implementing the survivorship care plan.* Seminars in Oncology Nursing, 2008. 24(3): p. 208-217.
57. Earle, C.C., *Failing to plan is planning to fail: improving the quality of care with survivorship care plans.* Journal of Clinical Oncology, 2006. 24(32): p. 5112-5116.
58. McCabe, M.S. and L. Jacobs, *Survivorship care: models and programs.* Seminars in Oncology Nursing, 2008. 24(3): p. 202-207.
59. Surgeons, A.C.o. *Cancer Program Standards 2012, Version 1.2.1: Ensuring Patient-Centered Care*. 2012 2012.
60. Academies, I.o.M.o.t.N., *From cancer patient to cancer survivor: lost in transition*. 2005.
61. Forsythe, L.P., et al., *Use of survivorship care plans in the United States: associations with survivorship care.* J Natl Cancer Inst, 2013. 105(20): p. 1579-87.
62. Mayer, D.K., et al., *American Society of Clinical Oncology clinical expert statement on cancer survivorship care planning.* J Oncol Pract, 2014. 10(6): p. 345-51.
63. Birken, S.A., et al., *Determinants of survivorship care plan use in US cancer programs.* J Cancer Educ, 2014. 29(4): p. 720-7.
64. Dulko, D., et al., *Barriers and facilitators to implementing cancer survivorship care plans.* Oncol Nurs Forum, 2013. 40(6): p. 575-80.
65. Brennan, M.E., et al., *Survivorship care plans in cancer: a systematic review of care plan outcomes.* Br J Cancer, 2014. 111(10): p. 1899-908.
66. Blanch-Hartigan, D., et al., *Provision and discussion of survivorship care plans among cancer survivors: results of a nationally representative survey of oncologists and primary care physicians.* J Clin Oncol, 2014. 32(15): p. 1578-85.
67. Hawkins, N.A., et al., *Examining Adherence With Recommendations for Follow-Up in the Prevention Among Colorectal Cancer Survivors Study.* Oncol Nurs Forum, 2015. 42(3): p. 233-40.
68. Playdon, M., et al., *Health information needs and preferences in relation to survivorship care plans of long-term cancer survivors in the American Cancer Society's Study of Cancer Survivors-I.* J Cancer Surviv, 2016.
69. Hill-Kayser, C.E., et al., *Feasibility Study of an Electronic Interface Between Internet-Based Survivorship Care Plans and Electronic Medical Records.* J Oncol Pract, 2016. 12(4): p. e380-7.
70. Zabora, J.R., et al., *The challenges of the integration of cancer survivorship care plans with electronic medical records.* Semin Oncol Nurs, 2015. 31(1): p. 73-8.
71. Alfano, C.M., et al., *An action plan for translating cancer survivorship research into care.* J Natl Cancer Inst, 2014. 106(11).
72. Boekhout, A.H., et al., *A survivorship care plan for breast cancer survivors: extended results of a randomized clinical trial.* J Cancer Surviv, 2015. 9(4): p. 683-91.
73. Faul, L.A., et al., *Associations among survivorship care plans, experiences of survivorship care, and functioning in older breast cancer survivors: CALGB/Alliance 369901.* J Cancer Surviv, 2014. 8(4): p. 627-37.
74. Grunfeld, E., et al., *Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer.* Journal of Clinical Oncology, 2011. 29(36): p. 4755-4762.
75. Hebdon, M., et al., *Transitioning patients to survivorship care: a systematic review.* Oncol Nurs Forum, 2014. 41(6): p. 615-25.
76. CE, H.-K., et al., *Impact of internet-based cancer survivorship care plans on health care and lifestyle behaviors.* Cancer, 2013. 119(21): p. 3854-3860.
77. Keesing, S., B. McNamara, and L. Rosenwax, *Cancer survivors' experiences of using survivorship care plans: a systematic review of qualitative studies.* J Cancer Surviv, 2015. 9(2): p. 260-8.
78. Klemanski, D.L., K.K. Browning, and J. Kue, *Survivorship care plan preferences of cancer survivors and health care providers: a systematic review and quality appraisal of the evidence.* J Cancer Surviv, 2016. 10(1): p. 71-86.
79. Mayer, D.K., et al., *Summing it up: an integrative review of studies of cancer survivorship care plans (2006-2013).* Cancer, 2015. 121(7): p. 978-96.
80. McCabe, M.S., et al., *Risk-based health care, the cancer survivor, the oncologist, and the primary care physician.* Semin Oncol, 2013. 40(6): p. 804-12.
81. Nicolaije, K.A., et al., *Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial.* J Clin Oncol, 2015. 33(31): p. 3550-9.
82. Palmer, S.C., et al., *Outcomes and satisfaction after delivery of a breast cancer survivorship care plan: results of a multicenter trial.* J Oncol Pract, 2015. 11(2): p. e222-9.
83. Sprague, B.L., et al., *Patient satisfaction with breast and colorectal cancer survivorship care plans.* Clin J Oncol Nurs, 2013. 17(3): p. 266-72.
84. Rosenberg, C.A., et al., *Promotion of self-management for post treatment cancer survivors: evaluation of a risk-adapted visit.* J Cancer Surviv, 2016. 10(1): p. 206-19.
85. Boyajian, R.N., et al., *Desired elements and timing of cancer survivorship care: one approach may not fit all.* J Oncol Pract, 2014. 10(5): p. e293-8.

86. O'Malley, D.M., et al., *Follow-up Care Education and Information: Identifying Cancer Survivors in Need of More Guidance.* J Cancer Educ, 2016. 31(1): p. 63-9.
87. Fredericks, S., G. Martorella, and C. Catallo, *A systematic review of web-based educational interventions.* Clin Nurs Res, 2015. 24(1): p. 91-113.
88. McAlpine, H., et al., *A systematic review of types and efficacy of online interventions for cancer patients.* Patient Educ Couns, 2015. 98(3): p. 283-95.
89. Kim, A.R. and H.A. Park, *Web-based Self-management Support Interventions for Cancer Survivors: A Systematic Review and Meta-analyses.* Stud Health Technol Inform, 2015. 216: p. 142-7.
90. Kuijpers, W., et al., *A systematic review of web-based interventions for patient empowerment and physical activity in chronic diseases: relevance for cancer survivors.* Journal of Medical Internet Research, 2013. 15(2): p. e37.
91. Grossman, P., et al., *A mindfulness-based program for improving quality of life among hematopoietic stem cell transplantation survivors: feasibility and preliminary findings.* Support Care Cancer, 2015. 23(4): p. 1105-12.
92. Blanch-Hartigan, D., K.D. Blake, and K. Viswanath, *Cancer survivors' use of numerous information sources for cancer-related information: does more matter?* J Cancer Educ, 2014. 29(3): p. 488-96.
93. Finney Rutten, L.J., et al., *Cancer-Related Information Seeking Among Cancer Survivors: Trends Over a Decade (2003-2013).* J Cancer Educ, 2016. 31(2): p. 348-57.
94. Shea-Budgell, M.A., et al., *Information needs and sources of information for patients during cancer follow-up.* Curr Oncol, 2014. 21(4): p. 165-73.
95. Jansen, F., et al., *Cancer survivors' perceived need for supportive care and their attitude towards self-management and eHealth.* Support Care Cancer, 2015. 23(6): p. 1679-88.
96. Attai, D.J., et al., *Twitter Social Media is an Effective Tool for Breast Cancer Patient Education and Support: Patient-Reported Outcomes by Survey.* J Med Internet Res, 2015. 17(7): p. e188.
97. Owen, J., E. Bantum, and A. Stanton, *Engagement with a Social Networking Intervention for Cancer-Related Distress.* Ann Behav Med, 2015. 49(2): p. 154-164.
98. Valle, C.G., et al., *A randomized trial of a Facebook-based physical activity intervention for young adult cancer survivors.* J Cancer Surviv, 2013. 7(3): p. 355-68.
99. Bantum, E.O., et al., *Surviving and thriving with cancer using a Web-based health behavior change intervention: randomized controlled trial.* J Med Internet Res, 2014. 16(2): p. e54.
100. Kjaer, T., et al., *Do we reach the patients with the most problems? Baseline data from the WebCan study among survivors of head-and-neck cancer, Denmark.* J Cancer Surviv, 2016. 10(2): p. 251-60.
101. Slev, V.N., et al., *Effects of eHealth for patients and informal caregivers confronted with cancer: A meta-review.* Int J Med Inform, 2016. 87: p. 54-67.
102. Cleary, E.H. and A.L. Stanton, *Mediators of an Internet-based psychosocial intervention for women with breast cancer.* Health Psychol, 2015. 34(5): p. 477-85.
103. Ritterband, L.M., et al., *Initial evaluation of an Internet intervention to improve the sleep of cancer survivors with insomnia.* Psycho-Oncology, 2012. 21(7): p. 695-705.
104. Schover, L.R., et al., *Efficacy trial of an Internet-based intervention for cancer-related female sexual dysfunction.* Journal of the National Comprehensive Cancer Network, 2013. 11(11): p. 1389-1397.
105. Smith, S.K., et al., *Evaluation of Pillars4life: a virtual coping skills program for cancer survivors.* Psychooncology, 2015. 24(11): p. 1407-15.
106. Stanton, A.L., et al., *Project connect online: randomized trial of an internet-based program to chronicle the cancer experience and facilitate communication.* Journal of Clinical Oncology, 2013. 31(27): p. 3411-3417.
107. Steel, J.L., et al., *Web-based collaborative care intervention to manage cancer-related symptoms in the palliative care setting.* Cancer, 2016. 122(8): p. 1270-82.
108. Willems, R.A., et al., *Short-term effectiveness of a web-based tailored intervention for cancer survivors on quality of life, anxiety, depression, and fatigue: randomized controlled trial.* Psychooncology, 2016.
109. Carpenter, K.M., et al., *An online stress management workbook for breast cancer.* J Behav Med, 2014. 37(3): p. 458-68.
110. Kanera, I.M., et al., *Lifestyle-related effects of the web-based Kanker Nazorg Wijzer (Cancer Aftercare Guide) intervention for cancer survivors: a randomized controlled trial.* J Cancer Surviv, 2016.
111. Northouse, L., et al., *A tailored Web-based psychoeducational intervention for cancer patients and their family caregivers.* Cancer Nurs, 2014. 37(5): p. 321-30.
112. Zernicke, K.A., et al., *A randomized wait-list controlled trial of feasibility and efficacy of an online mindfulness-based cancer recovery program: the eTherapy for cancer applying mindfulness trial.* Psychosom Med, 2014. 76(4): p. 257-67.
113. De Cocker, K., et al., *Development and usability of a computer-tailored pedometer-based physical activity advice for breast cancer survivors.* Eur J Cancer Care (Engl), 2015. 24(5): p. 673-82.
114. Moreira, H. and M.C. Canavarro, *A longitudinal study about the body image and psychosocial adjustment of breast cancer patients during the course of the disease.* European Journal of Oncology Nursing, 2010. 14(4): p. 263-270.
115. Ramachandra, P., et al., *A brief self-administered psychological intervention to improve well-being in patients with cancer: results from a feasibility study.* Psycho-Oncology, 2009. 18(12): p. 1323-1326.

116. Duffecy, J., et al., *Project onward: an innovative e-health intervention for cancer survivors.* Psycho-Oncology, 2012. 22(4): p. 947-951.
117. Duman-Lubberding, S., et al., *Feasibility of an eHealth application "OncoKompas" to improve personalized survivorship cancer care.* Support Care Cancer, 2016. 24(5): p. 2163-71.
118. Chen, Z., et al., *Dissecting an online intervention for cancer survivors: four exploratory analyses of internet engagement and its effects on health status and health behaviors.* Health Educ Behav, 2015. 42(1): p. 32-45.
119. Miller, S.M., et al., *Development and preliminary testing of PROGRESS: a Web-based education program for prostate cancer survivors transitioning from active treatment.* J Cancer Surviv, 2015. 9(3): p. 541-53.
120. Gorlick, A., E.O. Bantum, and J.E. Owen, *Internet-based interventions for cancer-related distress: exploring the experiences of those whose needs are not met.* Psychooncology, 2014. 23(4): p. 452-8.
121. Pellegrini, C.A., J. Steglitz, and S.A. Hoffman, *e-Health intervention development: a synopsis and comment on "What Design Features are Used in Effective e-Health Interventions? A Review Using Techniques From Critical Interpretive Synthesis".* Transl Behav Med, 2014. 4(4): p. 342-5.
122. Majhail, N.S., et al., *Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation.* Bone Marrow Transplant, 2012. 47(3): p. 337-41.
123. Murphy, E.A., et al., *Patient and provider preferences: Treatment summary and survivorship care plans after hematopoietic cell transplant.* Journal of Clincal Oncology, 2015. 34(Suppl 3S): p. 63.
124. Denzen, E.M., et al., *Patient and provider preferences for receiving treatment summary and survivorship care plans for allogeneic hematopoietic cell transplantation survivors: A qualitative study.* Biology of Blood and Marrow Transplantation, 2015. Suppl 1: p. S174-175.
125. Spain, P.D., et al., *Response to a treatment summary and care plan among adult survivors of pediatric and young adult cancer.* J Oncol Pract, 2012. 8(3): p. 196-202.
126. Mosca, L., et al., *Effectiveness-based guidelines for the prevention of cardiovascular disease in women--2011 update: a guideline from the american heart association.* Circulation, 2011. 123(11): p. 1243-62.
127. Unverzagt, S., et al., *Meta-regression analyses to explain statistical heterogeneity in a systematic review of strategies for guideline implementation in primary health care.* PLoS One, 2014. 9(10): p. e110619.
128. Syrjala, K.L., et al., *Development and implementation of an Internet-based survivorship care program for cancer survivors treated with hematopoietic stem cell transplantation.* Journal of Cancer Survivorship, 2011. 5(3): p. 292-304.
129. Syrjala, K.L., et al., *Internet-based randomized controlled trial (RCT) to meet survivorship needs of long-term hematopoietic stem cell transplantation recipients.* Fifth Biennial Cancer Survivorship Research Conference, 2010.
130. Syrjala, K., et al., *Efficacy of an internet RCT for long-term cancer survivors after hematopoietic cell transplantation (HCT).* Annals of Behavioral Medicine, 2013. 45(Supplement): p. S88.
131. Coffey, L., et al., *Cancer survivors' perspectives on adjustment-focused self-management interventions: a qualitative meta-synthesis.* J Cancer Surviv, 2016.
132. Foster, C., et al., *Managing fatigue after cancer treatment: development of RESTORE, a web-based resource to support self-management.* Psychooncology, 2015. 24(8): p. 940-9.
133. Lee, M.K., et al., *A Web-based self-management exercise and diet intervention for breast cancer survivors: pilot randomized controlled trial.* Int J Nurs Stud, 2014. 51(12): p. 1557-67.
134. van den Berg, S.W., et al., *BREATH: Web-Based Self-Management for Psychological Adjustment After Primary Breast Cancer--Results of a Multicenter Randomized Controlled Trial.* J Clin Oncol, 2015. 33(25): p. 2763-71.
135. Moody, L., et al., *Web-based self-management for young cancer survivors: consideration of user requirements and barriers to implementation.* J Cancer Surviv, 2015. 9(2): p. 188-200.
136. Morrison, L.G., et al., *What design features are used in effective e-health interventions? A review using techniques from Critical Interpretive Synthesis.* Telemed J E Health, 2012. 18(2): p. 137-44.
137. Dyer, G., et al., *What They Want: Inclusion of Blood and Marrow Transplanation Survivor Preference in the Development of Models of Care for Long-Term Health in Sydney, Australia.* Biol Blood Marrow Transplant, 2016. 22(4): p. 731-43.
138. Braamse, A.M., et al., *A randomized clinical trial on the effectiveness of an intervention to treat psychological distress and improve quality of life after autologous stem cell transplantation.* Ann Hematol, 2016. 95(1): p. 105-14.
139. Freeman, L.W., et al., *A randomized trial comparing live and telemedicine deliveries of an imagery-based behavioral intervention for breast cancer survivors: reducing symptoms and barriers to care.* Psychooncology, 2015. 24(8): p. 910-8.
140. Glasgow, R.E., et al., *Twelve-month outcomes of an Internet-based diabetes self-management support program.* Patient Education & Counseling, 2012. 87(1): p. 81-92.
141. Glasgow, R.E., et al., *Self-management aspects of the improving chronic illness care breakthrough series: implementation with diabetes and heart failure teams.* Annals of Behavioral Medicine, 2002. 24(2): p. 80-87.
142. Lorig, K., et al., *Online diabetes self-management program: a randomized study.* Diabetes Care, 2010. 33(6): p. 1275-1281.
143. Schulman-Green, D., et al., *Self-management and transitions in women with advanced breast cancer.* Journal of Pain & Symptom Management, 2011. 42(4): p. 517-525.

144. Ransom, S., P.B. Jacobsen, and M. Booth-Jones, *Validation of the Distress Thermometer with bone marrow transplant patients.* Psycho-Oncology, 2006. 15(7): p. 604-612.
145. Recklitis, C.J., et al., *Screening adult survivors of childhood cancer with the distress thermometer: a comparison with the SCL-90-R.* Psycho-Oncology, 2007. 16(11): p. 1046-1049.
146. Mitchell, A.J., *Pooled results from 38 analyses of the accuracy of distress thermometer and other ultra-short methods of detecting cancer-related mood disorders.* Journal of Clinical Oncology, 2007. 25(29): p. 4670-4681.
147. Lazenby, M., et al., *Comparing the distress thermometer (DT) with the patient health questionnaire (PHQ)-2 for screening for possible cases of depression among patients newly diagnosed with advanced cancer.* Palliat Support Care, 2014. 12(1): p. 63-8.
148. Schulz-Kindermann, F., et al., *The role of biomedical and psychosocial factors for the prediction of pain and distress in patients undergoing high-dose therapy and BMT / PBSCT.* Bone Marrow Transplantation, 2002. 29(4): p. 341-351.
149. McGregor, B.A., et al., *The effect of pre-transplant distress on immune reconstitution among adult autologous hematopoietic cell transplantation patients.* Brain Behav Immun, 2013. 30 Suppl: p. S142-8.
150. Jacobsen, P.B., et al., *Exercise and stress management training prior to hematopoietic cell transplantation: Blood and Marrow Transplant Clinical Trials Network (BMT CTN) 0902.* Biol Blood Marrow Transplant, 2014. 20(10): p. 1530-6.
151. Syrjala, K.L., et al., *Cancer and Treatment Distress (CTXD) Psychometric Evaluation over Time: a BMT CTN 0902 Secondary Analysis.* Cancer, 2016. in press.
152. Sirey, J.A., et al., *The Cornell Service Index as a measure of health service use.* Psychiatric Services, 2005. 56(12): p. 1564-1569.
153. Khera, N., et al., *Factors associated with adherence to preventive care practices among hematopoietic cell transplantation survivors.* Biol Blood Marrow Transplant, 2011. 17(7): p. 995-1003.
154. Syrjala, K.L., et al. *Adherence to health care surveillance guidelines and barriers to adherence in long-term cancer survivors who received hematopoietic cell transplantation (HCT)*. in *6th Biennial Cancer Survivorship Research: Translating Science to Care, co-sponsored by the National Cancer Institute, the American Cancer Society, LIVESTRONG, and the Centers for Disease Control and Prevention*. 2012. Washington DC.
155. Kroenke, K., et al., *The PHQ-8 as a measure of current depression in the general population.* Journal of Affective Disorders, 2009. 114(1-3): p. 163-173.
156. Unutzer, J., et al., *Collaborative care management of late-life depression in the primary care setting.* JAMA, 2002. 288(22): p. 2836-2845.
157. Mulrow, C.D., et al., *Case-finding instruments for depression in primary care settings.* Annals of Internal Medicine, 1995. 122(12): p. 913-921.
158. Godin, G., J. Jobin, and J. Bouillon, *Assessment of leisure time exercise behavior by self-report.* Canadian Journal of Public Health, 1986. 77: p. 359-361.
159. Syrjala, K.L., et al., *Measuring musculoskeletal symptoms in cancer survivors who receive hematopoietic cell transplantation.* J Cancer Surviv, 2010. 4(3): p. 225-35.
160. Artherholt, S.B., et al., *A comparison of physical activity measure in long-term cancer survivors.* Annals of Behavioral Medicine, 2010. 39(suppl): p. s99.
161. Courneya, K.S., M.R. Keats, and A.R. Turner, *Physical exercise and quality of life in cancer patients following high dose chemotherapy and autologous bone marrow transplantation.* Psycho-Oncology, 2000. 9(2): p. 127-136.
162. Jacobs, D.R., et al., *A simultaneous evaluation of ten commonly used physical activity questionnaires.* Medicine and Science in Sports Exercise, 1993. 25: p. 81-91.
163. (CDC)., C.f.D.C. and N.C.f.H.S. (NCHS). *National Health and Nutrition Examination Survey Questionnaire*. 2006: Hyattsville, MD.
164. (CDC)., C.f.D.C., *Behavioral Risk Factor Surveillance System Survey Questionnaire.* 2010: Atlanta, GA.
165. Okura, Y., et al., *Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure.* Journal of Clinical Epidemiology, 2004. 57: p. 1096-1103.
166. Louie, A.D., et al., *Validation of self-reported complications by bone marrow transplantation survivors.* Bone Marrow Transplantation, 2000. 25: p. 1191-1196.
167. Abbas, M.A., et al., *Primary lymphoma of the cervix in a heart transplant patient.* AJR Am J Roentgenol, 1996. 167(5): p. 1136-8.
168. Lee, S.J., et al., *Development and validation of a scale to measure symptoms of chronic graft-versus-host disease.* Biology of Blood & Marrow Transplantation, 2002. 8(8): p. 444-452.
169. Bandura, A., *Self-Efficacy: The Exercise of Control*. 1997, New York: W.H. Freeman and Company.
170. Schwarzer, R. and M. Jerusalem, *Generalized Self-Efficacy scale*, in *Measures in Helath Psychology: A User's Portfolio. Causal and Control Beliefs*, J. Weinman, S. Wright, and M. Johnston, Editors. 1995, NFER-NELSON: Windsor, UK. p. 35-37.
171. Mandelblatt, J.S., et al., *Economic evaluation alongside a clinical trial of psycho-educational interventions to improve adjustment to survivorship among patients with breast cancer.* J Clin Oncol, 2008. 26(10): p. 1684-90.

172. Chang, Y., et al., *Economic Evaluation Alongside a Clinical Trial of Telephone Versus In-Person Genetic Counseling for BRCA1/2 Mutations in Geographically Underserved Areas.* J Oncol Pract, 2016. 12(1): p. 59, e1-13.
173. Zou, G., *A modified poisson regression approach to prospective studies with binary data.* American Journal of Epidemiology, 2004. 159(7): p. 702-706.