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Randomized controlled trial of individualized treatment summary and survivorship care plans for hematopoietic cell transplantation survivors

by Navneet S. Majhail, Elizabeth Murphy, Purushottam Laud, Jaime M. Preussler, Ellen M. Denzen, Beatrice Abetti, Alexia Adams, RaeAnne Besser, Linda J. Burns, Jan Cerny, Rebecca Drexler, Theresa Hahn, Lensa Idossa, Balkrishna Jahagirdar, Naynesh Kamani, Alison Loren, Deborah Mattila, Joseph McGuirk, Heather Moore, Jana Reynolds, Wael Saber, Lizette Salazar, Barry Schatz, Patrick Stiff, John R. Wingard, Karen L. Syrjala, and K. Scott Baker

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Randomized controlled trial of individualized treatment summary and survivorship care plans for hematopoietic cell transplantation survivors

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ARTICLE SUMMARY

- Individualized survivorship care plans can be generated using clinical data routinely submitted to a central registry of HCT recipients
- These care plans reduced cancer and treatment distress and improved mental domain of QOL in a randomized study of long-term HCT survivors

ABSTRACT

Survivorship care plans may facilitate long-term care for cancer survivors, but their effectiveness has not been established in hematopoietic cell transplantation recipients. We evaluated the impact of individualized survivorship care plans on patient-reported outcomes among transplant survivors. Adult (≥18 years at transplant) survivors who were 1-5 years post-transplantation, proficient in English, and without relapse or secondary cancers were eligible for this multicenter randomized trial. Care plans were developed based on risk-factors and treatment exposures using patient data routinely submitted by transplant centers to the Center for International Blood and Marrow Transplant Research and published guidelines for long-term follow-up of transplant survivors. Phone surveys assessing patient-reported outcomes were conducted at baseline and 6-months. Primary endpoint was confidence in survivorship information, and secondary endpoints included cancer and treatment distress, knowledge of transplant exposures, health care utilization and health-related quality of life. Of 495 patients enrolled, 458 completed a baseline survey and were randomized (care plan=231, standard care=227); 200 (87%) and 199 (88%) completed the 6-month assessments, respectively. Patient characteristics were balanced in the two arms. Participants on care plan arm reported significantly lower distress scores at 6-months and an increase in the Mental Component Summary quality of life score assessed by the SF12 instrument. No effect was observed on the endpoint of confidence in survivorship information or other secondary outcomes. Provision of individualized survivorship care plans generated using registry data was associated with reduced distress and improved mental domain of quality of life among 1-5 year hematopoietic cell transplantation survivors. (clinicaltrials.gov NCT02200133)

INTRODUCTION

It is estimated that there will be 250,000 hematopoietic cell transplantation (HCT) survivors in the United States (US) by 2020.[1] Patients who survive the period of early complications and disease relapse, generally 1-2 years after transplantation, can expect high probability of subsequent long-term survival.[2-7] Although potentially cured of their underlying disease, HCT survivors continue to be at risk for late complications that can cause substantial morbidity, mortality, and functional deficits, and contribute to psychosocial and quality of life impairments.[8-23] Established survivorship guidelines provide a pragmatic approach to the long-term follow-up of autologous and allogeneic HCT survivors by recommending a minimum set of screening and preventive evaluations that need to be performed periodically post-transplantation.[24,25]

HCT survivors frequently do not receive or adhere to preventive care guidelines.[26-28] Many barriers contribute to the inadequate provision of coordinated patient-centric survivorship care in this patient population.[29-31] Among these barriers, lack of awareness of exposures and risks by patients is strongly associated with a lower likelihood of adherence to preventive care recommendations.[26] Additionally, both transplant and non-transplant providers cite lack of knowledge of late complication risks and of awareness of guidelines as barriers to providing adequate preventive care.[32] Finally, capacity limitations at transplant centers may impede provision and coordination of preventive care to HCT survivors.[29,33-35] Interventions to enhance patient awareness of preventive care could potentially enhance appropriate healthcare utilization and adherence to survivorship guidelines, although, this approach has not been previously tested.

A treatment summary and survivorship care plan (SCP) is a tool that provides cancer survivors with information on their cancer type, treatments and potential consequences, and recommendations regarding follow-up and preventive care. SCPs are generally accepted as an important component of cancer survivorship care.[36] Randomized trials of SCPs in cancer patients have primarily focused on providing information through in-person visit with patients or educating primary care providers, and evidence of their efficacy in enhancing various aspects of cancer survivorship care is generally negative.[37] They are also frequently underutilized for many reasons, including insufficient resources for their generation and implementation, and a paucity of evidence regarding an impact on patient outcomes.[38-42] The use and dissemination of SCPs in HCT survivors are hampered by similar challenges, and many transplant centers do not routinely provide patients with this tool. Furthermore, these barriers may be accentuated given the highly complex nature and unique exposures associated with the transplant procedure and challenges that exist in providing coordinated survivorship care.[29]

We hypothesized that a patient centered approach with a personalized SCP based on published guidelines for prevention of HCT-related late complications,[24,25] and generated using patient data routinely submitted by transplant centers in the US to an international clinical outcomes registry (Center for International Blood and Marrow Transplant Research [CIBMTR]) would increase patient awareness of recommended preventive care, which in turn would reduce distress, promote healthy behaviors, enhance healthcare utilization for appropriate preventive care, and improve health related quality of life (HRQOL). By using existing CIBMTR data, this approach would overcome several system-level barriers to providing survivorship care through transplant centers. Furthermore, it could serve as a template for a generalizable and efficient mechanism for

providing a patient-centric SCP to long-term HCT survivors who frequently are no longer under the care of transplant centers and are particularly vulnerable to gaps in preventive care. In a multicenter randomized controlled trial (RCT), we evaluated the efficacy of such an individualized SCP instrument generated using registry data and mailed to patients versus standard care on improving patient reported outcomes in adult HCT survivors who were 1-5 years after their transplantation.

METHODS

Supplemental materials detail study methods. Briefly, potentially eligible patients from 17 participating US centers were identified from the CIBMTR database and their data were used to generate a paper-based SCP that was personalized to their HCT specific exposures (see Supplemental Materials).[43] Patient eligibility criteria were kept broad and included patients who were 1-5 years post-transplant, ≥18 years at the time of HCT, with no evidence of disease relapse/progression or second cancers, and fluency in English; patients were eligible irrespective of transplant type (autologous or allogeneic), diagnosis, donor source or conditioning regimen. None of the participating centers had an existing mechanism for routinely providing SCPs to their patients. The RCT used a multi-center design with patient-level randomization to treatment (Figure 1), and was approved by Institutional Review Boards at the NMDP and each participating site. A random order list of survivors was generated and released in blocks to centers, who confirmed patient survival and accuracy of SCP related data. Centers contacted and consented patients and then informed the CIBMTR, who proceeded with the rest of the study procedures. The CIBMTR Survey Research Group (SRG) conducted a phone assessment within 30 days of receiving participant enrollment form. Patients were randomized 1:1 to the SCP or

control arm (with delayed SCP). Patients randomized to the SCP arm were express mailed an information letter and their printed SCP while patients on the control arm received an information letter only. SRG then contacted all enrolled patients by phone between 7-28 days of mailing study materials to conduct a health literacy assessment using the Newest Vital Sign.[44] During this contact, patients on the SCP arm were given the opportunity to address any questions about the content or use of their SCP. No further contact was made till the 6-month phone survey. The Confidence in Survivorship Information (CSI) was the primary endpoint (Supplemental Table 1).[45] Secondary endpoints focused on Cancer and Treatment Distress (CTXD),[20,46] as well as measures of Knowledge of Transplant Exposures, Health Care Utilization,[26] and HRQOL using the SF-12.[47] Patients on the intervention arm also received a 12-item assessment for qualitative feedback on SCP utilization. Sample size calculations were performed using a standard error formula that allowed for possible variability in treatment effect across centers and considered dropouts from baseline to 6 months. Our enrollment goal was 495 patients, which yielded adequate power to detect standardized effect sizes of ≥ 0.3, which are considered to be clinically meaningful, and anticipated a 10% drop-off from baseline to 6-months. An intention-to-treat approach was followed for analysis. A mixed model with center-level random effects and a fixed treatment effect was used to test whether a change in baseline and 6-month existed between the treatment and control groups for the primary and secondary endpoints. The 6-month assessment was used as a response variable and the baseline assessment was used as an explanatory variable in the regression models. If a treatment effect existed, we further evaluated whether the effect was modified by demographic variables or any interactions between variables.

RESULTS

Patient Characteristics

Among the 495 patients enrolled, 458 completed the baseline survey and were randomized (SCP=231, control=227); 200 (87%) and 199 (88%) completed 6-month assessments, respectively (Figure 2). The main reasons for dropout were loss to followup or patients not eligible for followup assessment due to interim disease relapse or progression. A greater proportion of patients who completed the 6-month assessment were White and reported higher health literacy scores; otherwise there were no significant differences in the demographic characteristics of patients who did and did not complete the 6-month assessments (Supplemental Table 2). Patient and transplant characteristics (including health literacy scores) were well balanced between the two arms, except for sex (49% males in SCP compared to 60% in controls, P=0.01) (Table 1). Median age was 59 years in both arms and enrolled patients were predominantly White (96% SCP and 92% controls). In the SCP and control arms, 48% and 44% had received allogeneic HCT; among allogeneic HCT recipients 63% and 67% had a history of acute GVHD and 60% and 66% had a history of chronic graft-versus-host disease (GVHD), respectively.

Analyses of Primary and Secondary Endpoints

Of the 458 patients randomized to the two arms, 399 completed 6-month assessments, including 398 who completed pre- and post-measurements for the primary endpoint (Table 2). We did not find any association between the SCP intervention and change in CSI scores from baseline to 6-months (P=0.223), even after assessing for the effect of demographic factors and interactions. However, we did observe a significant decrease in CTXD scores (P=0.004) and increase in

HRQOL Mental Component Summary (MCS) scores as assessed by SF-12 (P=0.003) among patients randomized to the SCP arm. There was no association between the SCP intervention and other secondary endpoints.

We further assessed the effect of demographic variables and interactions for the endpoints of CTXD and SF-12 MCS, where a significant treatment effect was observed. Age was significantly associated with CTXD scores (regression estimate -0.006, standard error 0.002; P=0.001), with lower distress among older patients. However, there was no significant interaction between age and SCP intervention and adjustment for age did not modify the treatment effect. The decrease in CTXD score for the SCP arm was independent of sex, health literacy, diagnosis, transplant type, and GVHD status (including acute and chronic GVHD). We also found a similar effect of age on MCS scores with older patients reporting significantly higher scores (estimate 0.03, standard error 0.034; P<0.001) and there was a significant interaction between age and SCP intervention (P=0.012). However, increase in mean MCS score in the SCP arm was independent of sex, health literacy, diagnosis, transplant type, and GVHD status.

Utilization of SCP

At their 6-month end-of-study assessments, patients on the intervention arm were asked questions about usefulness of the SCP for their survivorship care (Figure 3). A relatively large proportion of survivors reported that they found SCP somewhat or very useful for helping them better understand their HCT and related treatments (70%), side effects of HCT (65%), and managing their health (69%). The SCP helped survivors better communicate about HCT and its side effects with their medical providers. The 6-month interview included an open-ended

question about patients experience with the SCP; dominant themes identified on qualitative analyses included patients reporting that SCP helped survivors focus on their overall health, supported them in making care decisions with providers, and supported emotional health and coping.

DISCUSSION

In this large multicenter RCT of HCT survivors 1-5 years post-transplantation, we demonstrate that SCPs generated using a centralized clinical registry (CIBMTR), individualized to patient exposures, and without clinician contact to interpret or personalize their content and recommendations, are feasible and have desirable outcomes including lower treatment-related distress and improved mental health domain of HRQOL. Our results support further research towards broader implementation of our SCP instrument for facilitating care of HCT survivors and provides evidence to support a patient centered approach towards administration of SCPs.

SCPs have been endorsed as a tool for facilitating the care of cancer survivors with the goal of improving patient outcomes by promoting care-coordination, shared-decision making, self-management, and adherence to treatment recommendations.[36,48] Evidence on their efficacy in impacting patients outcomes is mixed, and SCPs have not been universally adopted due to other barriers such as lack of standardized templates, need for extensive resources and time for their generation, and lack of reimbursement for their implementation.[42,48-50] Similar challenges exist for transplant centers, and many programs have capacity limitations that frequently prevent provision of personalized comprehensive SCPs to their patients. Our SCP procedure provides several advantages to patients and transplant centers. It uses data that centers routinely submit

electronically to the CIBMTR and will provide a resource-effective mechanism for centers to generate the SCP for their recipients. Instead of receiving a generic SCP, patients can receive one that is specific to their treatment exposures. Our approach of facilitating patient ownership of survivorship care is different from the prevalent non-transplant cancer literature where SCPs have been largely tested in the setting of clinicians providing them to patients.[37] Our SCP instrument was in a paper-based format and mailed to patients; more general dissemination would require its translation into an electronic format. Hence, further research is still needed to guide its implementation. An ongoing project funded by the National Cancer Institute is investigating its use in combination with an online health informatics platform to facilitate a self-management program for selected late complications among HCT survivors (NCT03125070; Syrjala, Baker and Majhail).

Of note, we did not observe any impact of the SCP intervention on our primary endpoint of CSI. Our study population consisted of HCT survivors who were relatively early post-transplantation (1-5 years) and enrolled by centers with an interest in providing survivorship care to their transplant recipients; it is possible our instrument may be more effective in enhancing knowledge and confidence about follow-up care among patients who are further out from transplantation or those who are not followed primarily or closely by their transplant centers. The CSI instrument has been validated in cancer survivors but not among HCT recipients, and it is also possible that it did not adequately measure the underlying construct in our patient population. The six-month pre- and post-intervention follow-up period was most likely too short to detect any significant associations with changes in healthcare adherence or utilization. We did not observe any interaction of GVHD with the intervention and study outcomes. This was most likely due to our

study population being relatively further out from transplantation and the short duration of the intervention. Furthermore, it is likely that patients with GVHD were under the active care of transplant centers and this may have impacted patient reported outcomes assessed in our study (e.g., greater confidence in recommended care, less distress, etc.). These same factors were probably responsible for some patients not finding the SCP tool to be useful for various aspects of survivorship care (see Figure 3; "*I have not done this*" and "*Not at all useful*" responses on SCP utilization survey administered as part of end-of-study assessments for the intervention arm).

The concordant findings of reduction in CTXD scores and improvement in SF-12 MCS scores cross-validate the overall effect of SCP on reducing distress and improving HRQOL in our study population of HCT survivors. It is important to note that these effects occurred over a relatively short period of time and did not require any additional clinical contact or intervention to facilitate the use of the SCP. Interestingly, we found an independent association between older age and lower CTXD scores, which is consistent with other literature where older adults are less distressed about cancer and survivorship.[51-54] The SCP provided concise information on previous treatments and potential late effects, and practical guidance regarding recommended preventive care that survivors could easily understand and share, which may have empowered them in the CTXD domains (e.g., uncertainty, health burden and medical demands) and MCS domains (e.g., mental health, social functioning, role-emotional), leading to the improvement in those areas.[55]

Some limitations of our study must be acknowledged. First, the treatment summary portion of our SCP primarily included HCT-related and post-transplant events and did not have detailed

information on pre-transplant exposures as those data are not captured comprehensively by the CIBMTR. However, transplant centers have the option to add information about those exposures to the basic template of the SCP. Participants who completed 6-month assessments were more likely White and had higher health literacy, which may limit the generalizability of our findings. However, this is reflective of the prevailing healthcare disparities in HCT and research on other interventions to facilitate SCP use in this underserved population is needed.[56] Notwithstanding these limitations, the pragmatic nature of our study eligibility criteria and schema will make our results broadly applicable to transplant centers in the US.

An ideal mechanism to provide SCPs to HCT survivors would involve a dynamic, adaptable, and patient-specific shared-decision making approach between patients, their transplant centers, and other providers. However, several challenges prevent centers from providing this tool to facilitate survivorship care for their patients and SCPs that can be generated efficiently and without requiring significant center resources would be impactful for patient care. Our study supports further implementation of an individualized SCP generated using CIBMTR data in a population of HCT survivors that is at significant risk for late morbidity and mortality. Future research will examine the role of the SCP instrument in preventing specific late complications, in facilitating care coordination, and will serve as a platform for investigating novel methods for survivorship care delivery and implementation.

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Drafting of Manuscript: Navneet Majhail, Jaime Preussler, Purushottam Laud

Critical Review and Final Approval of Manuscript: All authors

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Table 1. Baseline characteristics of patients enrolled on the study

Characteristic	SCP (N=231)	Routine care (N=227)
Age at HCT, years; Median (range)	59 (19-81)	59 (20-77)
Time from HCT to enrollment (months); Median (range)	42 (16-66)	45 (16-66)
Age group at baseline survey, years; N (%)		
18-29	7 (3)	9 (4)
30-39	10 (4)	14 (6)
40-49	28 (12)	18 (8)
50-59	55 (24)	58 (26)
60-69	83 (36)	92 (41)
≥70	48 (21)	36 (16)
Sex; N (%)		
Male	112 (49)	136 (60)
Female	119 (52)	91 (40)
Ethnicity; N (%)		
Hispanic/Latino	8 (3)	7 (3)
Non-Hispanic/Latino	216 (94)	216 (95)
Declined	7 (3)	4 (2)
Race; N (%)		
White	222 (96)	208 (92)
African-American	5 (2)	15 (7)
Asian	2 (1)	3 (1)
Pacific Islander	1 (<1)	0 (0)
Declined	1 (<1)	1 (<1)
Diagnosis; N (%)		
Acute myeloid leukemia	52 (23)	46 (20)
Acute lymphoblastic leukemia	10 (4)	8 (4)
Myelodysplastic/myeloproliferative disorders	19 (8)	23 (10)
Chronic myeloid leukemia	2 (1)	3 (1)
Hodgkin lymphoma	13 (6)	10 (4)
Non-Hodgkin lymphoma	49 (21)	47 (21)
Plasma cell disorder/multiple myeloma	78 (34)	80 (35)
Other	8 (3)	10 (4)
Time from diagnosis to HCT, months; Median (range)	7 (1-266)	8 (1- 327)
Year of transplant; N (%)		
2010	11 (5)	22 (10)
2011	67 (29)	61 (27)
2012	48 (21)	53 (23)
2013	81 (35)	64 (28)
2014	24 (10)	27 (12)

Transplant type; N (%)		
Allogeneic	111 (48)	100 (44)
Autologous	120 (52)	127 (56)
Donor type; N (%)		
Allogeneic, related	47 (20)	36 (16)
Allogeneic, unrelated/umbilical cord blood	64 (28)	64 (28)
Autologous	120 (52)	127 (56)
Graft type; N (%)		
Bone marrow	15 (7)	16 (7)
Peripheral blood	207 (90)	203 (89)
Umbilical cord blood	9 (4)	8 (4)
Number of transplants; N (%)		
1	206 (89)	191 (84)
≥2	25 (11)	36 (16)
Conditioning regimen intensity; N (%)		
Myeloablative (including autologous regimens)	168 (73)	176 (78)
Non-myeloablative/Reduced-intensity	62 (27)	50 (22)
Missing	1 (<1)	1 (<1)
TBI as part of conditioning regimen; N (%)		
Yes	49 (21)	46 (20)
No	182 (79)	181 (80)
History of acute GVHD; N (%)*		
Yes	70 (63)	67 (67)
No	41 (37)	33 (33)
History of chronic GVHD; N (%)*		
Yes	67 (60)	66 (66)
No	44 (40)	34 (34)
Health Literacy; N (%)†		
Adequate literacy	154 (74)	172 (83)
Possibility of limited literacy	36 (17)	27 (13)
High likelihood of limited literacy	18 (9)	9 (4)

SCP – survivorship care plan; HCT – hematopoietic cell transplantation; TBI – total body irradiation; GVHD – graft-versus-host disease

* Allogeneic HCT only
† Assessed by Newest Vital Sign instrument; N=208 for SCP arm and N=208 for routine care arm

Table 2: Analysis for primary and secondary endpoints

Endpoint*		Mean (Standard Deviation)		Estimate (Standard Error)#	P-value#
		Baseline	6-months		
Confidence in Survivorship Information†	SCP (N=199)	1.44 (0.34)	1.50 (0.34)	-0.034 (0.028)	0.223
	Routine care (N=199)	1.40 (0.38)	1.44 (0.39)		
Cancer and Treatment Distress‡	SCP (N=199)	0.91 (0.61)	0.78 (0.59)	0.123 (0.042)	0.004
	Routine care (N=198)	0.91 (0.64)	0.91 (0.69)		
Knowledge of Transplant Exposures†	SCP (N=200)	0.86 (0.18)	0.87 (0.16)	-0.018 (0.013)	0.182
	Routine care (N=198)	0.88 (0.15)	0.86 (0.16)		
Health Care Utilization†	SCP (N=200)	0.80 (0.14)	0.80 (0.15)	0.014 (0.010)	0.149
	Routine care (N=198)	0.80 (0.14)	0.82 (0.13)		
SF12: Physical Component Summary†	SCP (N=200)	46.1 (10.3)	46.2 (10.6)	-0.368 (0.638)	0.565
	Routine care (N=198)	46.0 (9.8)	45.8 (10.1)		
SF12: Mental Component Summary†	SCP (N=200)	53.9 (7.6)	54.7 (7.0)	-8.907 (3.009)	0.003
	Routine care (N=198)	53.9 (7.9)	53.4 (8.8)		

* N represents number who completed both baseline and 6-month assessments

Estimate and P-value based on analysis of covariance model with center-level random effects where any differences between the treatment groups were measured after adjustment for patients' baseline measurement; where applicable, estimates were adjusted for demographic variables and/or interactions (see Methods section)

† Higher score better

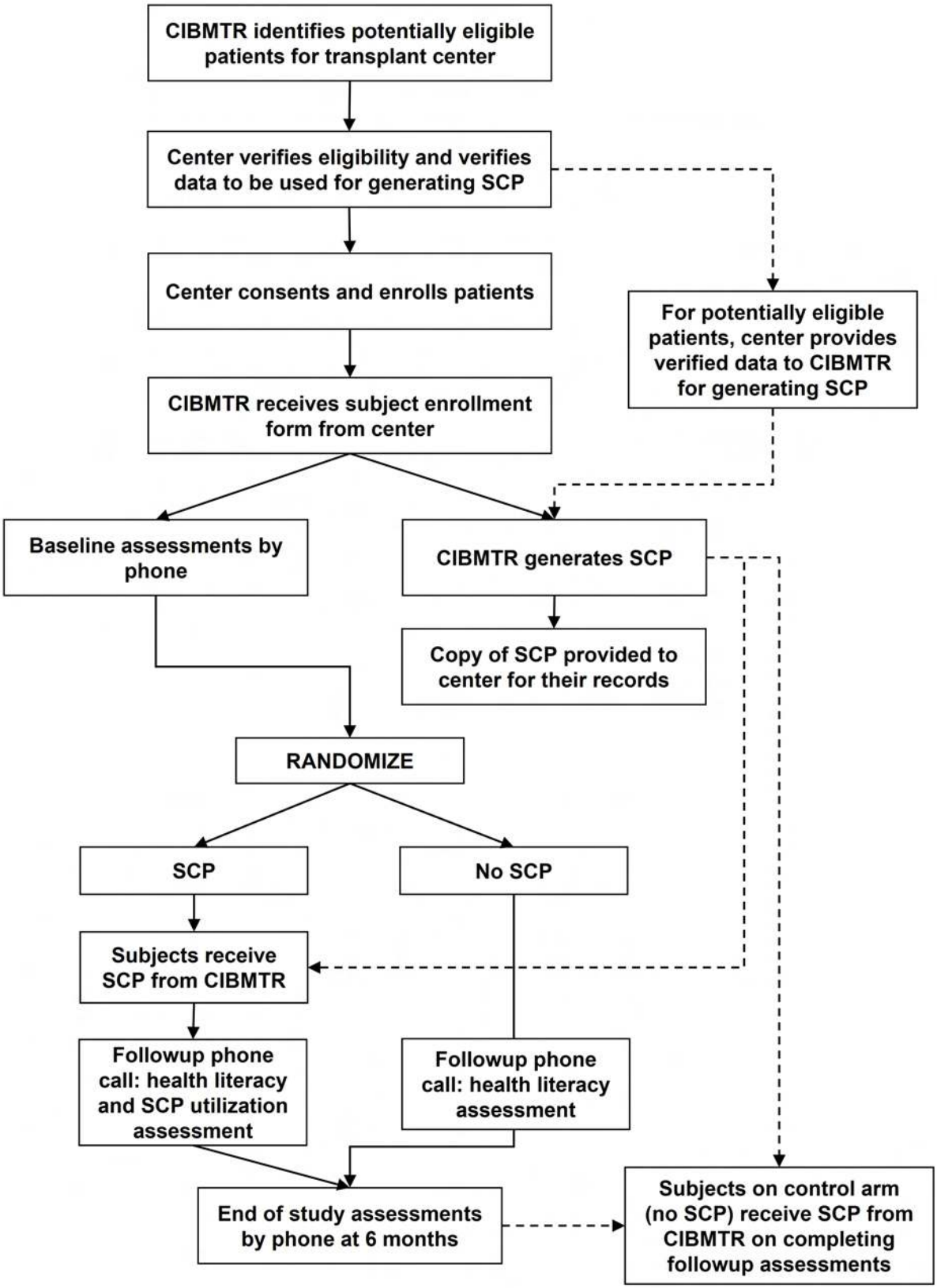
‡ Lower score better

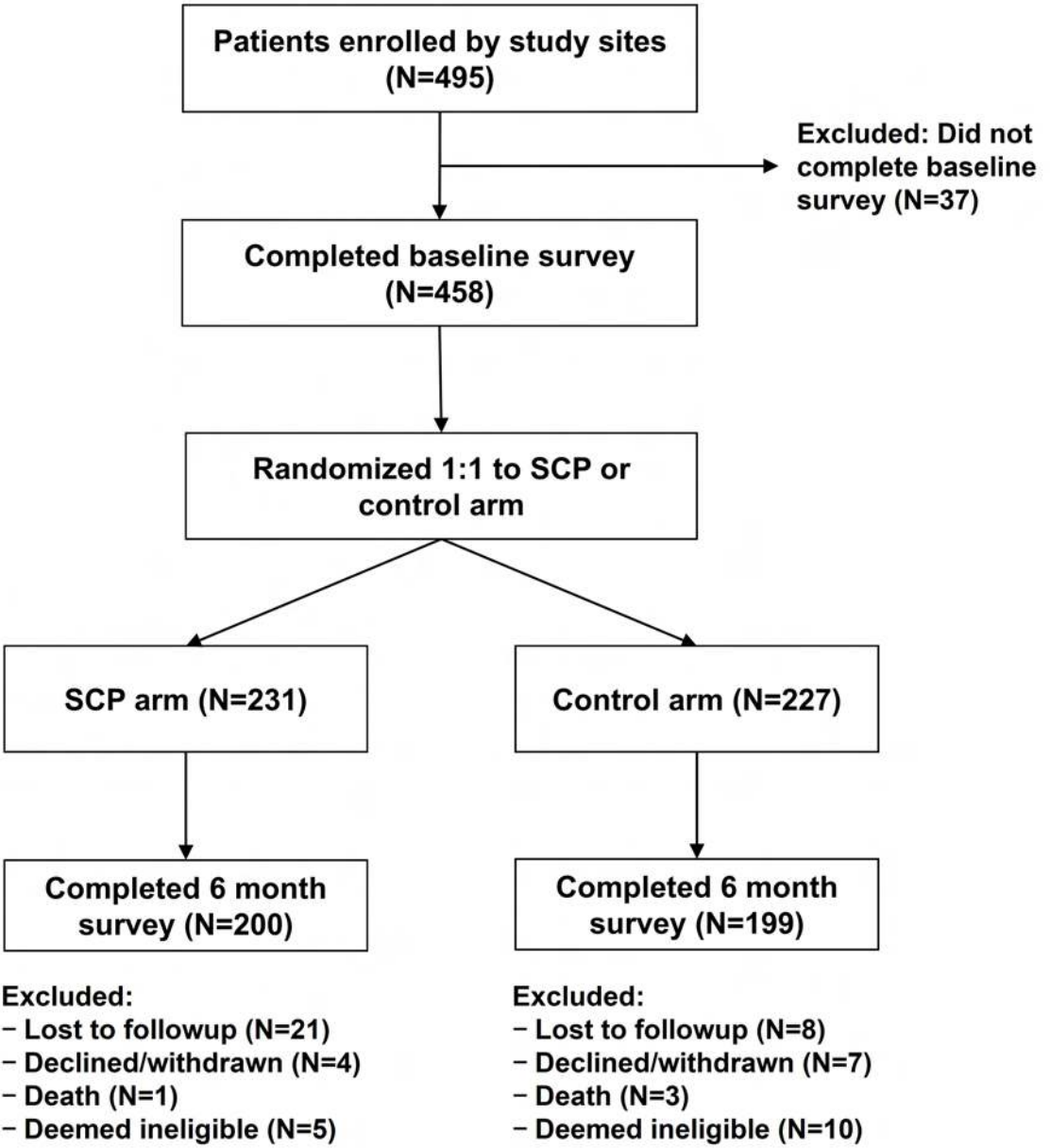
FIGURE LEGENDS

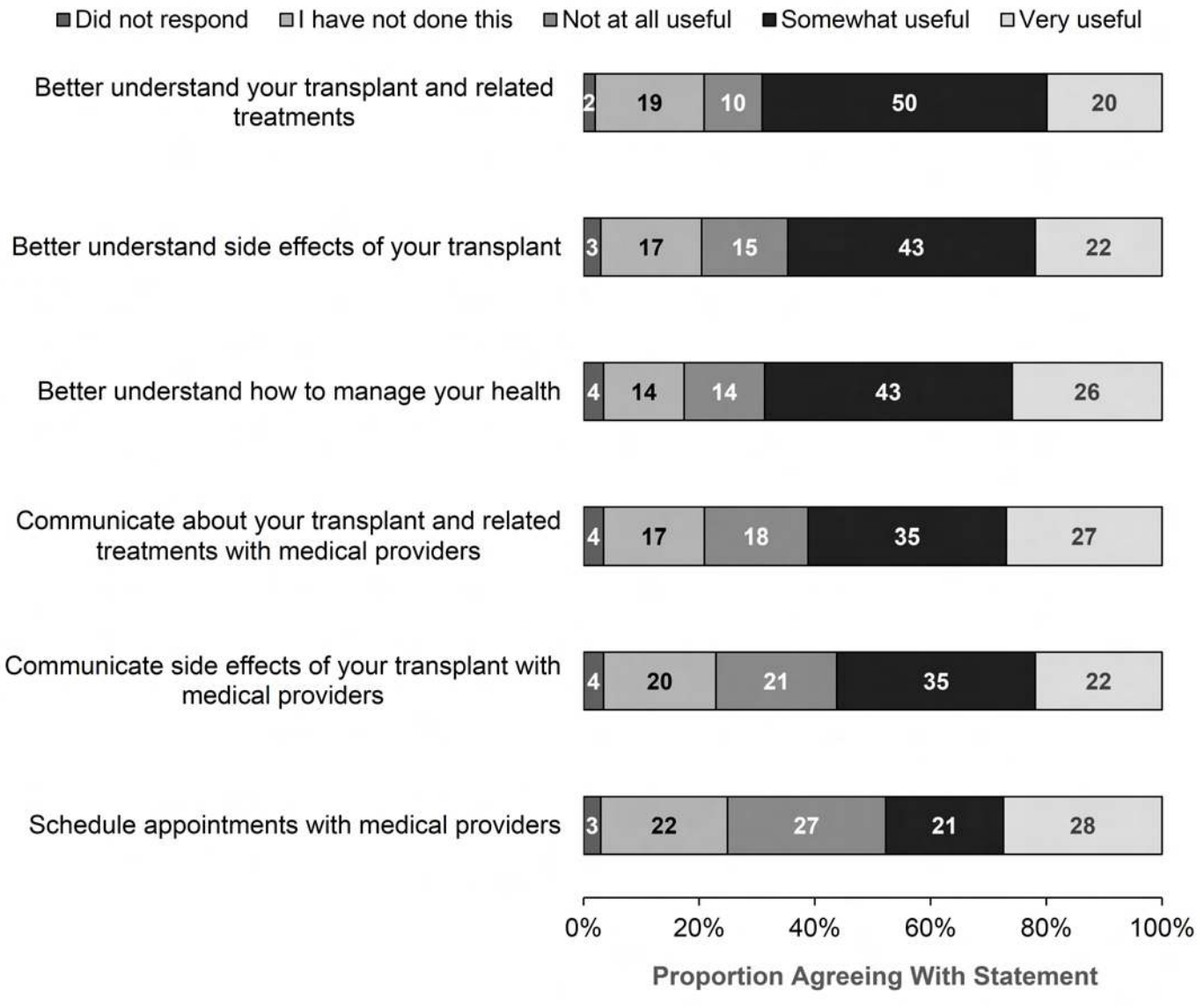
Figure 1: Study schema

Figure 2: CONSORT diagram

Figure 3: Patient reported assessment of usefulness of SCP intervention (N=201 respondents on SCP arm who completed 6-month end-of-study assessments)


CIBMTR identifies potentially eligible patients for transplant center
Center verifies eligibility and verifies data to be used for generating SCP
Center consents and enrolls patients
CIBMTR receives subject enrollment form from center
For potentially eligible patients, center provides verified data to CIBMTR for generating SCP
Baseline assessments by phone
CIBMTR generates SCP
Copy of SCP provided to center for their records
RANDOMIZE
SCP
No SCP
Subjects receive SCP from CIBMTR
Followup phone call: health literacy and SCP utilization assessment
Followup phone call: health literacy assessment
End of study assessments by phone at 6 months
Subjects on control arm (no SCP) receive SCP from CIBMTR on completing followup assessments


Patients enrolled by study sites (N=495)
Excluded: Did not complete baseline survey (N=37)
Completed baseline survey (N=458)
Randomized 1:1 to SCP or control arm
SCP arm (N=231)
Control arm (N=227)
Completed 6 month survey (N=200)
Completed 6 month survey (N=199)
Excluded:
− Lost to followup (N=21)
− Declined/withdrawn (N=4)
− Death (N=1)
− Deemed ineligible (N=5)
Excluded:
− Lost to followup (N=8)
− Declined/withdrawn (N=7)
− Death (N=3)
− Deemed ineligible (N=10)


Did not respond
I have not done this
Not at all useful
Somewhat useful
Very useful
Better understand your transplant and related treatments
2
19
10
50
20
Better understand side effects of your transplant
3
17
15
43
22
Better understand how to manage your health
4
14
14
43
26
Communicate about your transplant and related treatments with medical providers
4
17
18
35
27
Communicate side effects of your transplant with medical providers
4
20
21
35
22
Schedule appointments with medical providers
3
22
27
21
28
0%
20%
40%
60%
80%
100%
Proportion Agreeing With Statement

SUPPLEMENTAL MATERIALS

Randomized Trial of Individualized Treatment Summary and Survivorship Care Plan for Hematopoietic Cell Transplantation Survivors

DETAILED METHODS

Patients

Seventeen US transplant centers that report autologous and allogeneic HCT to the CIBMTR and representing diverse location and size participated in the study. Potentially eligible patients from participating centers were identified from the CIBMTR. The CIBMTR is a research collaboration between the National Marrow Donor Program (NMDP)/Be The Match in Minneapolis, Minnesota and the Medical College of Wisconsin in Milwaukee, Wisconsin. By law in the US, transplant centers are required to submit data on all allogeneic HCTs to the CIBMTR. Additionally, approximately 80% of the national autologous HCT activity is captured by the registry. Computerized checks for discrepancies, physicians' review of submitted data and on-site audits of participating centers ensure data quality. Centers submit Transplant Essential Data (TED) on all recipients before transplant, at 100 days and six months after transplant, annually until 6 years, and every other year thereafter, or until death. These data were used to generate the treatment summary including information on patient diagnosis and stage, donor and graft source, and transplantation procedure (e.g., conditioning regimen). HCT specific exposures that determine follow-up and preventive evaluations (age, sex, transplant type, exposure to total body irradiation [TBI], exposure to corticosteroids, and graft-versus-host disease [GVHD]) were abstracted from TED and were used to develop the personalized care plan for each patient.

To maximize generalizability, patient eligibility criteria were intentionally kept broad (≥18 years at the time of HCT, recipients of autologous or allogeneic transplantation, with no evidence of relapse, disease progression or secondary cancers, any diagnosis, donor or graft source, and any conditioning regimen). Patients had to be 1-5 years from their transplant, in order to focus on a group of survivors who are frequently no longer under the direct care of transplant centers and are most vulnerable to receive inadequate HCT specific-survivorship and preventive care. Participants could have received more than one HCT. Participants had to be fluent in English so that they could complete study assessments.

Only centers without an existing mechanism for routinely providing SCPs to their patients were invited to participate in our study. Information on prevalent practices for caring for autologous and allogeneic HCT long-term survivors, including templates for discharge summaries and any routine communications with patients and their local providers, was requested form centers and was reviewed by study investigators to confirm their eligibility to participate and enroll patients. Participating centers also committed to not providing patients a SCP during routine post-transplant care and outside the context of this study during the enrollment and follow up period.

SCP Template

We have previously reported on the development of an individualized SCP instrument generated using CIBMTR registry data and specifically targeted for use by HCT survivors.[1] Briefly, a draft paper-based template for the SCP was generated by the investigators and consisted of three elements: an introductory page with information on appropriate use of the SCP, a treatment summary with diagnosis and transplant information electronically abstracted from CIBMTR data, and a care plan that listed recommended preventive evaluations based on published guidelines and patient specific exposures (age, sex, transplant type, exposure to TBI or steroids, or occurrence of GVHD). To obtain qualitative feedback on content and formatting of the SCP,

phone focus groups were conducted with HCT survivors/caregivers (3 focus groups, N=22 participants), HCT physicians and advanced practice providers (2 focus groups, N=14 participants), hematology-oncology and primary care physicians and advanced practice providers (3 focus groups, N=24 participants), and HCT nurses and social workers (4 focus groups, N=17 participants). Qualitative analyses identified patient-centered elements that informed the generation of the final SCP templates used as the intervention in the RCT.[1] A sample SCP template is available as part of Supplemental Materials.

Study Procedures

The RCT used a multi-center design with patient-level randomization to treatment (Figure 1). The RCT was reviewed and approved by Institutional Review Boards (IRBs) at the NMDP and each participating site and was registered on clinicaltrials.gov (NCT02200133). To minimize bias in patient enrollment, a random order list of potentially eligible 1-5 year survivors for each center was generated using the CIBMTR database and released in blocks of 10-20 patients. Center coordinators then reviewed medical records to confirm patient survival, disease status, and accuracy of SCP related research data that had been submitted by the center to the CIBMTR. Centers contacted patients by phone and presented the study, and then mailed an information packet to patients who agreed to consider participation; some center IRBs required a mailed letter/post-card with an opt in/opt out option, followed by mailing of the information packet to patients who opted in or with follow-up phone calls if no response to the mailing was received. On receiving the signed informed consent form from patients, transplant centers informed the CIBMTR, who then proceeded with the rest of the study procedures.

The CIBMTR Survey Research Group (SRG) conducted a baseline assessment by phone within 30 days of receiving a completed participant enrollment form and contact information from the transplant center. CIBMTR data were then used to generate personalized SCPs for all consenting patients. Patients were randomized 1:1 to either the SCP arm or standard care with delayed SCP (control) arm. Since centers may preferentially follow long-term allogeneic HCT survivors, patient enrollment was weighted such that at least one-third of the cohort consisted of autologous HCT recipients. Patients randomized to the SCP arm were express mailed an information letter and their printed SCP from the CIBMTR, while patients on the control arm received only an information letter. All patients received a phone call from the CIBMTR SRG between 7-28 days of mailing study materials to conduct a health literacy assessment using the Newest Vital Sign.[2] During this phone contact, patients on the SCP arm were also given the opportunity to ask and address any questions about the content or use of their SCP. No further contact was made with patients till their 6-month outcomes phone survey conducted by the CIBMTR SRG. After completing their end-of-study assessments, printed SCPs were provided to patients in the control arm. Study accrual began in April 2015 and the last patient was enrolled in June 2016. Patients were not offered any compensation for participating on the study.

Assessments

Supplemental Table 1 describes our study instruments, including their psychometric properties. The Confidence in Survivorship Information (CSI) was the primary endpoint. The CSI is a 13-item questionnaire that uses a 3-point Likert scale of “not at all” to "very confident”.[3] The instrument has two subscales, one that tests confidence in knowledge of past cancer diagnostic and treatment details (3 items, Cronbach’s α=0.77) and second that evaluates confidence in

knowledge about prevention and treatment of long-term and late-effects of disease and treatment, prevention of disease recurrence, access to resources, and familial risk of cancer (10 items, Cronbach's α=0.95). Internal consistency reliability for the CSI in our HCT sample at baseline was α=0.87. Secondary endpoints focused on Cancer and Treatment Distress (CTXD), a 23 item instrument validated in HCT recipients that assesses distress and worry specific to HCT and associated complications,[4,5] as well as measures of Knowledge of Transplant Exposures (developed by study investigators), Health Care Utilization,[6] and HRQOL using the SF-12.[7] The phone-administered assessments required 30-45 minutes to complete. Patients on the intervention arm also received an investigator developed 12-item assessment that obtained qualitative feedback on patient utilization of the SCP at the 6-month assessment.

Statistical Analysis

Sample size and power calculations were performed using a standard error formula that allowed for possible variability in treatment effect across centers and considered dropouts from baseline to 6 months. Our targeted enrollment goal was 495 patients, which yielded adequate power to detect standardized effect sizes of ≥0.3, which are considered to be clinically meaningful, and anticipated a 10% drop-off from baseline to 6-months. An intention-to-treat approach was followed for analysis.

Baseline characteristics between the two groups were compared using Chi-square tests for categorical variables and t-tests for continuous variables. A mixed model with center-level random effects and a fixed treatment effect was used to test whether a change in baseline and 6-month existed between the treatment and control groups for the primary and secondary endpoints. The model, in addition to accounting for center-to-center variation (center effect), allowed for patient responses to be correlated within centers. The 6-month assessment was used as a response variable and the baseline assessment was used as an explanatory variable in the regression models. If a treatment effect existed, we further evaluated whether the effect was modified by demographic variables (including age, sex, transplant type, acute and/or chronic GVHD, diagnosis, and health literacy), or any interactions between variables. Given the short time period projected for accrual and the low risk of adverse events, no interim analyses were planned. Analyses were performed using SAS software (Version 9.4). All P-values reported are two-sided and $P<0.05$ was considered significant.

Data Sharing Statement

The study was funded by Patient Centered Outcomes Research Institute (PCORI), and their data sharing policy applies (www.pcori.org).

References for Methods

1. Denzen EM, Preussler JM, Murphy EA, et al. Tailoring a survivorship care plan: Patient and provider preferences for recipients of hematopoietic cell transplantation *Biol Blood Marrow Transplant*. 2018;(In press).
2. Weiss BD, Mays MZ, Martz W, et al. Quick assessment of literacy in primary care: the newest vital sign. *Ann Fam Med*. 2005;3(6):514-522.

3. Palmer SC, Jacobs LA, Mao J, Stricker CT. Are cancer survivors confident in their knowledge about their disease and care. *Cancer Survivorship Research: Translating Science to Care*. 2012:A32.
4. Syrjala KL, Chapko ME. Evidence for a biopsychosocial model of cancer treatment-related pain. *Pain*. 1995;61(1):69-79.
5. Syrjala KL, Langer SL, Abrams JR, et al. Recovery and long-term function after hematopoietic cell transplantation for leukemia or lymphoma. *JAMA*. 2004;291(19):2335-2343.
6. Khera N, Chow EJ, Leisenring WM, et al. Factors associated with adherence to preventive care practices among hematopoietic cell transplantation survivors. *Biol Blood Marrow Transplant*. 2011;17(7):995-1003.
7. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care*. 1996;34(3):220-233.

Supplemental Table 1: Study assessments and patient reported outcome measures

Instrument	Description	Items	Time point	Estimated Time to complete
Confidence in Survivorship Information (CSI)[1]	Assesses confidence in knowledge of past cancer diagnostic/treatment details and confidence in knowledge about prevention/treatment of late complications, prevention of future disease, access to resources and familial risk of cancer. This 13-item patient self-reported tool assesses confidence in knowledge of past cancer diagnostic and treatment details (3 items; Cronbach's alpha = 0.77) and confidence in knowledge about prevention and treatment of long term and late-effects of disease and treatment, prevention of future disease, access to resources, and familial risk of cancer (10 items; Cronbach's alpha = 0.95). The scale uses a 3-point scale ranging from "not at all" to "very confident" in each knowledge item. Sample items include "I am confident in the stage of cancer I have/had" and "I am confident in strategies for treating long term physical effects of cancer". Higher score indicates greater confidence in knowledge of treatment details and preventive recommendations.	13	Baseline 6 mos	2 mts
Cancer and Treatment Distress (CTXD)[2-5]	Assesses distress or worry specific to HCT and associated complications using items such as “costs of healthcare”, “possibility of relapse” and “being a burden to other people”; subscales include uncertainty, family strain, medical system demands, health burden, finances and impact on function. Response options can range from 0 (“none”) to 3 (“severe”), and the scores represent the mean response across the scale/subscale item. In an analysis of 701 HCT recipients, Syrjala et al reported strong internal consistency reliability at pre-transplant, and at day 100 and day 180 post-transplant (Cronbach α 0.94, 0.95 and 0.95, respectively). The mean scores (standard deviation) at the three time points were 1.12 (0.60), 0.93 (0.60), and 0.85 (0.59), respectively. Subscale reliability was high across time (α >0.70), and there was strong correlation of pre-transplantation CTXD with post-transplant CTXD. A higher score indicates higher level of distress among HCT recipients. Testing supports its value as a predictor of health outcomes and it has been in several randomized clinical trials.	27	Baseline 6 mos	3 mts
Knowledge of transplant exposures	Investigator developed measure to assess knowledge of HCT exposures (conditioning type, TBI use, transplant type, donor type, GVHD). Higher score indicates greater knowledge of transplant exposures.	5	Baseline 6 mos	2 mts
Health Behaviors	Standardized measures to assess health behaviors: Godin Leisure Time Exercise Q as a measure of minutes/week in moderate/vigorous activity (<150 as cutoff);[6] Tobacco use (any as cutoff); [7,8] Alcohol use (≥ 1 drinks/day for women, ≥ 2 drinks/day for men as cutoff);[7,8] Sunscreen use (daily use of >SPF 30 sunscreen as cutoff);[7,8] Diet (>2 fast food meals/week and <5 fruits and vegetables/day as cutoff);[7,8] Body Mass Index (>30 as cutoff)[7,8] Health behaviors are	31	Baseline 6 mos	8 mts

	scored as a sum from 0-7, with one point for each behavior: non-smoking, alcohol less than one glass a day for women or two glasses a day for men, moderate to vigorous physical activity ≥ 150 minutes a week, regular use of sunscreen of SPF ≥ 30, food intake of 5 servings of fruit and vegetables a day, body mass index ≤ 25, sleep averaging ≥ 7 hours a night. Item content is matched to NHANES or BRFSS for normative comparisons. Higher scores indicate positive health care behaviors.			
Health Care Utilization[9]	Widely pretested measure of SCP recommended screening and preventive evaluations; scores range from 0-15 with 2 gender specific items each. Scores are transformed to the proportion preventive care recommendations met as indicated on the SCP. Higher scores indicate greater and appropriate health care utilization for preventive care.	26	Baseline 6 mos	4 mts
SF-12[10,11]	Validated health quality of life 12-item sub-set of the MOS SF-36 which accurately reproduces the two summary component scores: Physical Component Summary Score (PCS) and Mental Health Component Summary Score (MCS). In the general population, the test-retest reliability has been reported to be 0.89 and 0.76 for the two scores, respectively. Studies have shown that the relative validity of SF-12 is comparable to the more comprehensive SF-36 quality of life instrument. The mean PCS scores for chronic health conditions are in the range of 40-45, while that for MCS range from 50-55; in comparison, the mean general population PCS and MCS scores are ~50 and ~50, respectively. Higher scores correspond to better health-related quality of life.	12	Baseline 6 mos	3 mts
Generalized Self-Efficacy scale[12,13]	Assesses optimistic self-beliefs used to cope with a variety of demands in life known as self-efficacy, i.e., the belief that one's actions are responsible for successful outcomes. The scaled score for each question ranges from 1 to 4. Higher scores indicate stronger patient's belief in self-efficacy.	10	Baseline 6 mos	2 mts
Newest Vital Sign[14]	Measures health literacy level using 1 scenario of an ice cream container nutrition label; 1 score (6 items) includes assessment of two main constructs, numeracy and reading comprehension. Higher score indicates greater health literacy.	6	1-4 wks	2 mts
Survivorship Care Plan Utilization Assessment	Treatment-group participants will be asked whether they if they have any questions about the SCP and how they plan to use it. At the 6 month follow-up assessment, treatment-group participants will be asked how they did use their SCP and what they liked or did not like about it.	5	1-4 wks 6 mos	3 mts

HCT – hematopoietic cell transplantation; TBI – total body irradiation; GVHD – graft-versus-host disease; SCP – treatment summary and survivorship care plan; mos – months; mts – minutes

References for study assessments:

1. Palmer SC, Jacobs LA, Mao J, Stricker CT. Are cancer survivors confident in their knowledge about their disease and care. *Cancer Survivorship Research: Translating Science to Care*. 2012:A32.

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Supplemental Table 2. Baseline characteristics of patients who completed the baseline assessments, and then either completed the study or dropped out/were excluded from the analysis

Characteristic	Completed study (N=399)	Drop out/ excluded (N=59)	P-value
Age at HCT, years; Median (range)	58.8 (19.4-81.1)	54.5 (20.2-77.2)	0.6760
Time from HCT to enrollment (months); Median (range)	42.6 (15.7-66.3)	45.3 (17.3-63.8)	0.6760
Age group at baseline survey, years; N (%)			
18-29	12 (3.0)	4 (6.8)	0.1755
30-39	19 (4.8)	5 (8.5)	
40-49	41 (10.3)	5 (8.5)	
50-59	99 (24.8)	14 (23.7)	
60-69	159 (39.9)	16 (27.1)	
≥70	69 (17.3)	15 (25.4)	
Sex; N (%)			
Male	212 (53.1)	36 (61.0)	0.2667
Female	187 (46.9)	23 (39.0)	
Ethnicity; N (%)			
Hispanic/Latino	13 (3.3)	2 (3.4)	0.4346
Non-Hispanic/Latino	375 (94.0)	57 (96.6)	
Declined	11 (2.8)	-	
Race; N (%)			
White	380 (95.2)	50 (84.8)	0.0062
African-American	12 (3.0)	8 (13.6)	
Asian	4 (1.0)	1 (1.7)	
Pacific Islander	1 (0.3)	-	
Declined	2 (0.5)	-	
Diagnosis; N (%)			
Acute myeloid leukemia	90 (22.6)	8 (13.6)	0.0801
Acute lymphoblastic leukemia	15 (3.8)	3 (5.1)	
Myelodysplastic/myeloproliferative disorders	40 (10.0)	2 (4.8)	
Chronic myeloid leukemia	5 (1.3)	-	
Hodgkin lymphoma	16 (4.0)	7 (11.9)	
Non-Hodgkin lymphoma	84 (21.1)	12 (20.3)	
Plasma cell disorder/multiple myeloma	134 (33.6)	24 (40.7)	
Other	15 (3.8)	3 (5.1)	
Time from diagnosis to HCT, months; Median (range)			
Year of transplant; N (%)			
2010	28 (7.0)	5 (8.5)	0.5831
2011	112 (28.1)	16 (27.1)	
2012	86 (21.6)	15 (25.4)	
2013	125 (31.3)	20 (33.9)	
2014	48 (12.0)	3 (5.1)	

Transplant type; N (%)			
Allogeneic	191 (47.9)	20 (33.9)	0.0503
Autologous	208 (52.1)	39 (66.1)	
Donor type; N (%)			
Allogeneic, related	77 (19.3)	6 (10.2)	0.0975
Allogeneic, unrelated/umbilical cord blood	114 (28.6)	14 (23.7)	
Autologous	208 (52.1)	39 (66.1)	
Graft type; N (%)			
Bone marrow	29 (7.3)	2 (3.4)	0.4685
Peripheral blood	356 (89.2)	54 (91.5)	
Umbilical cord blood	14 (3.5)	3 (5.1)	
Number of transplants; N (%)			
1	347 (87.0)	50 (84.8)	0.6809
≥2	52 (13.0)	9 (15.3)	
Conditioning regimen intensity; N (%)			
Myeloablative (including autologous regimens)	296 (74.2)	48 (81.4)	0.4533
Non-myeloablative/Reduced-intensity	101 (25.3)	11 (18.6)	
Missing	2 (0.5)	-	
TBI as part of conditioning regimen; N (%)			
Yes	87 (21.8)	8 (13.6)	0.1449
No	312 (78.2)	51 (86.4)	
History of acute GVHD; N (%)*			
Yes	123 (64.4)	14 (70.0)	0.8062
No	68 (35.6)	6 (30.0)	
History of chronic GVHD; N (%)*			
Yes	119 (62.3)	14 (70.0)	0.6288
No	72 (37.7)	6 (30.0)	
Health Literacy; N (%)†			
Adequate literacy	309 (80.1)	17 (56.7)	0.0112
Possibility of limited literacy	54 (14.0)	9 (30.0)	
High likelihood of limited literacy	23 (6.0)	4 (13.3)	

SCP – survivorship care plan; HCT – hematopoietic cell transplantation; TBI – total body irradiation; GVHD – graft-versus-host disease

* Allogeneic HCT only

† Assessed by Newest Vital Sign instrument; N=386 for those retained and N=30 for those who dropped out/were excluded from the analysis

Supplemental Appendix: Sample template for treatment summary and survivorship care plan used in the study.

Blood and Marrow Transplant Survivor Treatment Summary

For: [First name_Last name]

Date Your Treatment Summary was Created: [Month DD, YYYY]

The information presented on this Treatment Summary comes from transplant-related data provided to the CIBMTR by your transplant center. There may be additional medical history that is relevant to you and important to share with your doctors and other medical care providers.

Your Medical Information
Date of birth: (text date)
Sex:
Diagnosis:
Date of Diagnosis: (date)
Your Transplant Information
Transplant center name:
Address: (hospital)
Phone number: (BMT program number)
Date of transplant: (date)
Age at transplant: (yrs)
Transplant type: (autologous/allogeneic unrelated/allogeneic related)
Cell source type: (bone marrow, peripheral stem cell, cord blood unit(s))
Prior transplant: (yes/no)
Date of most recent previous transplant: (date or not applicable)
Type of most recent previous transplant: (autologous / allogeneic / syngeneic(twin) or not applicable)

Patient CIBMTR research ID (**CRID**):

NMDP IRB Approved September 17, 2015
V7.0

Your Transplant Treatment
Chemotherapy drugs received as part of the preparative regimen: (list or not applicable)
Steroid drugs received as part of the preparative regimen (for example, prednisone): (list or not applicable)
Total Body Irradiation (TBI): (list dose and dose unit (cGy, Gy)/Yes/No)
Graft versus Host Disease (GVHD)
Drugs to prevent GVHD: (yes/no/not applicable)
GVHD prevention drugs: (list or not applicable)
Acute GVHD: (yes/no/ not applicable)
Chronic GVHD: (yes/no/ not applicable)
Date of chronic GVHD diagnosis: (text date or not applicable)

Your Blood and Marrow Transplant Survivorship Care Plan

Your survivorship care plan is based on research[1] and was developed by doctors and researchers from around the world. This information is not intended as medical advice and does not replace your transplant doctor's recommendations. **Your doctor may recommend or order other tests or evaluations on a different schedule based on your specific situation. Follow his or her recommendations carefully.**

In the table below, you'll find information on the tests and evaluations that physicians commonly recommend for transplant recipients after transplant. Items in **bold** are found in the Glossary.

The information below will help you:

- Understand what to expect at your checkup appointments, and
- Discuss your questions or concerns with your doctor.

There are questions you can ask your doctor to help you prepare for these tests and exams. Also, these questions will help you understand what the test results mean for you.

Some questions to ask your doctors

- Which tests and evaluations do I need to have more often? How often?
- How should I prepare for my exam? How long will the tests take?
- How long does it take to learn my test results?
- Are my test results within an acceptable range for my age and situation?
- How do I know when to call the clinic about symptoms I'm having?

Your care plan is organized by parts of the body (for example, eyes, mouth, and heart). Each section includes more questions to ask your doctor that are specific to a body part. There is space for you to take notes in each section and at the end of the care plan.

You should share this care plan with your doctors. Also, if you need to go to urgent care or the emergency room, it is helpful to take the care plan with you.

[1] Majhail NS, Rizzo JD, Lee SJ, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation; Center for International Blood and Marrow Transplant Research (CIBMTR), American Society for Blood and Marrow Transplantation (ASBMT), European Group for Blood and Marrow Transplantation (EBMT), Asia-Pacific Blood and Marrow Transplantation Group (APBMT), Bone Marrow Transplant Society of Australia and New Zealand (BMTSANZ), East Mediterranean Blood and Marrow Transplantation Group (EMBMT) and Sociedade Brasileira de Transplante de Medula Ossea (SBTMO). Co-published in Biol Blood Marrow Transplant. 2012; 18(3): 348-371; Bone Marrow Transplant (2012) 47, 337–341; and Hematol Oncol Stem Cel Ther 2012;5(1):1-30.

Summary of Recommendations for Your Preventive Care

Immune System

- ☐ Vaccines to prevent infection
- ☐ Because you have a history of **GVHD** and if you are on **immunosuppressant drugs**, you might need to take antibiotics to prevent infections like **pneumonia** and **meningitis**, for as long as you are on immunosuppressant drugs, and before dental work
- ☐ If you are on immunosuppressant drugs, you may need a test for **Cytomegalovirus (CMV).**

Eyes

- ☐ Wear sunglasses every time you go outside.
- ☐ Vision screening by your eye doctor 1 time every year to check how well you can see
- ☐ Because you have a history of GVHD, you may need to have eye exams more often

Mouth

- ☐ Because you have a history of GVHD and/or have received total body irradiation, you need to have mouth, teeth, tongue, and throat exam at least 2 times every year. Talk to your doctor and dentist about when you should have these check-ups.
- ☐ Dental exam and tooth cleaning by a dentist at least 1 time every year. Ask your doctor if you should take antibiotics before dental exams.

Lungs

- ☐ Lung exam at least 1 time every year
- ☐ Because you have a history of GVHD, you might need to have lung exams and pulmonary function tests more often. Talk to your doctor about when you should have these check-ups.
- ☐ Don't smoke or use tobacco. Stay away from places where people usually smoke.

Heart and Blood Vessels

Blood pressure checked every time you visit the clinic

- ☐ Blood tests to check your cholesterol level at least 1 time every year. This includes triglycerides, **LDL**, and **HDL**

Liver

- ☐ **Liver function blood tests** (to see if your liver is working well) at least 1 time every year

This information is not intended as medical advice and <u>does not</u> replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

- ☐ If you had red blood cell transfusions, have a blood ferritin test to check the level of iron in your blood.

KIDNEYS AND BLADDER

- ☐ Blood pressure checked every time you visit the clinic
- ☐ Kidney test at least 1 time every year which includes testing: protein levels in your urine and nitrogen levels in your blood (BUN) and creatinine test
- ☐ Because you have a history of GVHD, you might need to have your kidneys checked more often.

MUSCLES AND JOINTS

- ☐ If you have **myopathy** (weak muscles), muscle pain, or joint pain, schedule an appointment with your doctor right away. Your doctor will check your muscles to find out if you need treatment.
- ☐ Because you have a history of GVHD and have taken steroids (such as prednisone), you may need clinical tests of muscle strength and range of motion in your joints

BONES

- ☐ **Bone density scan** (test) every year.

SKIN

- ☐ Do a self-exam of your skin every month to check for any changes (for example, rash, unusual growth, or patch).
- ☐ Use sunscreen with SPF 15 or higher every time you go outside. Reapply at least every 2 hours, or more often if you're sweating or in and out of the water.
- ☐ Avoid direct sunlight. Wear a broad-brimmed hat or use a large umbrella to protect your skin.

NERVOUS SYSTEM

- ☐ Clinical exam by your doctor at least 1 time every year to check for changes or problems

ENDOCRINE ORGANS (THYROID, GROWTH AND SEX HORMONES)

- ☐ Blood test to check how well your **thyroid** is working
- ☐ Blood tests to assess your sex hormone levels
- ☐ Fasting glucose (sugar) test to check for Diabetes

GENITALS AND SEXUAL HEALTH

This information is not intended as medical advice and does not replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

- ☐ Discuss with your physician if you are experiencing sexual side effects such as vaginal dryness, pain with sex, or difficulty having an erection.
- ☐ Gynecology exam at least 1 time every year

Fertility and Family Planning

- ☐ If you want to have children in the future, ask your doctor to refer you to a **fertility** doctor.

Emotional health

- ☐ Going through transplant is a very emotional experience. Your feelings and needs will change a lot, maybe even every day. It's important that you talk openly and regularly with your doctor, family and friends.

Diet and nutrition

- ☐ Eat a healthy diet
- ☐ Keep yourself well hydrated
- ☐ Avoid foods with lots of processed (fake) sugar or saturated (bad) fat like candy or soda

General Health

- ☐ Use alcohol in moderation (less than 2 drinks a day)
- ☐ Stay physically active (2.5 hours each week of moderate exercise)
- ☐ Don't smoke, stay away from second hand smoke, don't use chewing tobacco

New cancer screening

Talk to your doctor about:

- ☐ Breast cancer screening (**mammography** every 1 to 2 years starting at age 25)
- ☐ Cervical cancer screening
- ☐ Colorectal cancer screening (starting at age 50 or earlier if you have a family history of colorectal cancer)
- ☐ Skin cancer screening

This information is not intended as medical advice and does not replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

Your Blood and Marrow Transplant Survivorship Care Plan

For: [First name_Last name]

RECOMMENDATIONS FOR YOUR ROUTINE SCREENING AND PREVENTIVE CARE	
IMMUNE SYSTEM	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
Even 5 years or more after transplant, you are at risk to get infections. This is because it takes time for your immune system to recover from transplant. You might also take medications that lower your body's ability to fight disease. ☐ Vaccines to prevent infection ☐ Because you have a history of **GVHD**, you might need to take antibiotics: • To prevent infections like **pneumonia** and **meningitis**, for as long as you are on immunosuppressant drugs • Before dental work ☐ If you are on immunosuppressant drugs, you may need a blood test for **Cytomegalovirus (CMV)** screening.	• What things can I do to lower the risk of getting an infection? Ask your doctor about things like water, food, safe sex, travel, and avoiding second hand smoke. • Are my vaccines up-to-date?
EYES	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
☐ Wear sunglasses every time you go outside. ☐ Vision screening by your eye doctor 1 time every year to check how well you can see ☐ Because you have a history of GVHD, you may need to have eye exams more often.	• Do I need to see an eye specialist? • How often should I have eye tests?

This information is not intended as medical advice and <u>does not</u> replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

RECOMMENDATIONS FOR YOUR ROUTINE SCREENING AND PREVENTIVE CARE	
☐ If you have eye pain, dryness, change in vision, sensitivity to light, or watery eyes, you need to have an eye exam. Your doctor will tell you if you need treatment.	
MOUTH	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
It's important that you brush and floss everyday to prevent infections. Also, your doctor needs to check your mouth to make sure your teeth, tongue and throat are healthy and there are no signs of **oral cancer**. ☐ General mouth, teeth, tongue, and throat exam at least 1 time every year ☐ Because you have a history of GVHD, you need to have mouth, teeth, tongue, and throat exams at least 2 times every year. Talk to your doctor and dentist about when you should have these check-ups. ☐ Because you had total body irradiation (TBI), you need to have mouth, teeth, tongue, and throat exams at least 2 times every year. Talk to your doctor about when you should have these check-ups. ☐ Dental exam and tooth cleaning by a dentist at least 1 time every year ☐ Tell your doctor and dentist if you have dry mouth. This could be a side effect of medications you are taking or a sign of GVHD.	• Other than not smoking, and brushing and flossing every day, are there other things I can do to keep my mouth healthy? • Do I need to take medicine before I have any dental procedures?
LUNGS	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**

This information is not intended as medical advice and does not replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

Recommendations For Your ROUTINE SCREENING AND Preventive Care

- ☐ Lung exam at least 1 time every year

If you have problems breathing or have had breathing problems in the past, you may need more tests such as:

- ☐ **Pulmonary function tests**
- ☐ Chest x-ray
- ☐ CT scan
- ☐ Because you have a history of GVHD, you might need to have lung exams and pulmonary function tests more often. Talk to your doctor about when you should have these check-ups.
- ☐ Don't smoke or use tobacco. Stay away from places where people usually smoke.

- What can I do to minimize my risk of getting infections?
- What tests should I have and how often?
- What can I do to help me quit smoking?

Heart and Blood Vessels

Questions to ask your doctor and your notes

Even many years after transplant heart problems can occur.

- ☐ Blood pressure checked every time you visit the clinic (also see Kidneys and Bladder section)
- ☐ Blood tests to check your cholesterol level at least 1 time every year. This includes triglycerides, **LDL**, and **HDL**

You may need these tests more often if you had heart or blood vessel problems before or after transplant.

- How can I minimize my risk of heart disease?
- My goals:
  - Blood pressure: _____
  - Cholesterol: _____
  - Weight: _____

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RECOMMENDATIONS FOR YOUR ROUTINE SCREENING AND PREVENTIVE CARE	
LIVER	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
☐ **Liver function blood tests** (to see if your liver is working well) at least 1 time every year ☐ If you had red blood cell transfusions, you may need to have a blood ferritin test to check the level of iron in your blood. • If you have too much iron in your blood or your test results are abnormal, your doctor might do more tests. • If you have a hepatitis B or C infection, your doctor will watch it closely.	• Do I need any other tests to make sure my liver is working well? • Do I need to see a liver specialist?
KIDNEYS AND BLADDER	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
☐ Blood pressure checked every time you visit the clinic. High blood pressure (hypertension) can damage your kidneys. ☐ Kidney test at least 1 time every year which includes testing: • Protein levels in your urine • Nitrogen levels in your blood (BUN) and creatinine test If your test results show that your kidneys are not working properly, you might need further tests such as: ☐ Kidney ultrasound ☐ Kidney biopsy If you have **kidney disease**, you should:	• What are things I can do now to keep my blood pressure in check? • If my blood pressure is high, what can I do to get it under control? • Do I need to see a kidney specialist? How often?

This information is not intended as medical advice and does not replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

RECOMMENDATIONS FOR YOUR ROUTINE SCREENING AND PREVENTIVE CARE	
☐ Avoid medicines and substances (foods, herbs, vitamin supplements) that can hurt your kidneys ☐ See a kidney doctor ☐ Because you have a history of GVHD, you might need to have your kidneys checked more often. Also, you can get urinary tract infections (UTI) more often.	
MUSCLES AND JOINTS	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
☐ If you have **myopathy** (weak muscles), muscle pain, or joint pain, schedule an appointment with your doctor right away. Your doctor will check your muscles to find out if you need treatment. Because you have a history of GVHD and have taken steroids (such as prednisone), talk to your doctor about clinical exam for: ☐ Muscle strength ☐ **Range of motion** in your joints	• Do I need to see a physical therapist? • How can I build my muscle strength?
BONES	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
Transplant can cause low levels of bone density. You can develop bone diseases if your density levels get too low (such as **osteopoenia** and **osteoporosis**). As a woman and because you've had an allogeneic transplant and taken steroids, you're more likely to have low levels of bone density. To help keep your bones healthy, you need to have: ☐ **Bone density scan** (test) every year. If your scan is abnormal, you might need more scans.	• Do I need a bone density scan at all? If so, how often? • What are the ways to help me prevent bone density loss?

This information is not intended as medical advice and does not replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

RECOMMENDATIONS FOR YOUR ROUTINE SCREENING AND PREVENTIVE CARE	
SKIN	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
☐ Do a self-exam of your skin every month to check for any changes (for example, rash, unusual growth, or patch). • If you see unusual growth or patch on your skin, tell your doctor as soon as possible. Your doctor will refer you to a skin specialist. ☐ Use sunscreen with SPF 15 or higher every time you go outside. Reapply at least every 2 hours, or more often if you're sweating or in and out of the water. ☐ Avoid direct sunlight. Wear a broad-brimmed hat or use a large umbrella to protect your skin from the sun.	• How do I do a self-exam of my skin? • Should I use any special soaps or lotions? • Do I have **scleroderma**? **Fasciitis**?
NERVOUS SYSTEM	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
The nervous system includes your brain, spinal cord and nerves. Sometimes after transplant, patients have changes or problems with how their nervous system works. ☐ Clinical exam by your doctor at least 1 time every year to check for changes or problems ☐ Tell your doctor right away if you have trouble with things like your memory, concentration, or making decisions. Your doctor will tell you if you need more tests and/or treatment.	• How do I know when to call the clinic about symptoms I'm having?
ENDOCRINE ORGANS (THYROID, GROWTH AND SEX HORMONES)	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**

This information is not intended as medical advice and does not replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

RECOMMENDATIONS FOR YOUR ROUTINE SCREENING AND PREVENTIVE CARE	
To make sure your endocrine system is working well, you should have these tests at least 1 time every year: ☐ Blood test to check how well your **thyroid** is working ☐ Blood tests to assess your sex hormone levels ☐ Fasting glucose (sugar) test to check for Diabetes (where you do not eat or drink anything before the test) You might need to see an OB/GYN (women's health doctor) to talk about hormone replacement therapy.	• Do I need to see an OB/GYN specialist?
GENITALS AND SEXUAL HEALTH	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
☐ To stay healthy you should have a gynecology exam at least 1 time every year Tell your doctor if you have any of these symptoms: ☐ Low sex drive ☐ Erectile dysfunction or impotence ☐ Hot flashes ☐ Vaginal dryness ☐ Vaginal pain or bleeding after sexual intercourse These could be signs of low sex hormone levels, menopause or GVHD. You might go into early menopause after transplant, even if you're young. Your doctor will tell you if you need more tests and/or treatment.	• Should I do a breast/testicular self exam? How often? What should I be looking for? • Do I need to be tested for sexually transmitted diseases? • How can I stay sexually healthy after transplant?

This information is not intended as medical advice and <u>does not</u> replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

RECOMMENDATIONS FOR YOUR ROUTINE SCREENING AND PREVENTIVE CARE	
FERTILITY AND FAMILY PLANNING	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
Transplant can lower your ability to have children. ☐ Ask your doctor about your chances of being able to have children after transplant. ☐ If you want to have children in the future, ask your doctor to refer you to a **fertility** doctor. ☐ Talking about fertility can be very emotional. See the Emotional Health section for ways to help you sort out your feelings.	• Should my partner or I be using birth control? • What type of birth control is best for my partner or me?
EMOTIONAL HEALTH	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
Going through transplant is a very emotional experience. Your feelings and needs will change a lot, maybe even every day. It's important that you talk openly and regularly with your doctor, family and friends. Here are some questions to help you sort out your feelings and talk about them with people you trust: • How do you feel overall? Better or worse than expected? How do you feel today? How is it different from how you felt yesterday? • Are you worried or angry about anything? • Are you eating well? • How is your energy level? Are you tired more often or do you easily become tired? Are you sleeping well?	• What can I do to make sure I'm taking care of myself emotionally? • Should I see another doctor, therapist, or counselor about my emotional health? • Are there any counseling or support groups in my area that I could join?

This information is not intended as medical advice and does not replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

RECOMMENDATIONS FOR YOUR ROUTINE SCREENING AND PREVENTIVE CARE	
• Have you noticed if anything makes you feel better or worse? • How are your relationships with your loved one/partner/spouse? Family? Close friends? Are you talking with them about any relationship problems? • Are you asking for help when you need it?	
DIET AND NUTRITION	**QUESTIONS TO ASK YOUR DOCTOR AND YOUR NOTES**
To stay healthy and help your immune system fight disease, eat a healthy diet that includes many different foods. General guidelines for a balanced diet include: □ Vegetables, fruits and whole grains - 2-3 cups every day □ Protein - 3-6 ounces every day of cooked lean meats like fish and chicken (or 46-56 grams of protein) □ Dairy 3 cups every day (low-fat or fat-free) □ Drink at least eight 8-ounce glasses of fluid every day to stay hydrated. You need to drink more water when: • It's hot outside • You exercise or are more physically active • You have a fever or diarrhea or vomit (throw up) □ Avoid foods with lots of processed (fake) sugar or saturated (bad) fat like candy or soda After transplant, you might experience changes in taste, loss of appetite, nausea or other symptoms that make it hard to keep a healthy diet. Talk to your doctor about your symptoms.	• Should I see a dietician (diet and nutrition expert)? • Should I be concerned about any new allergies? • If I have trouble with GVHD of my **GI tract**, can you help me make a plan to maintain a healthy diet? • How can I keep a healthy diet and weight?

This information is not intended as medical advice and <u>does not</u> replace your transplant doctor's recommendations. Your doctor may recommend or order other tests or evaluations based on your specific situation. Follow his or her recommendations carefully.

Recommendations For Your ROUTINE SCREENING AND Preventive Care

General Health	Questions to ask your doctor and your notes
It's important to take care of yourself and follow your doctor's orders to stay healthy and well. To make sure you are staying healthy overall, follow these general lifestyle practices: ☐ Use alcohol in moderation (less than 2 drinks a day) ☐ Stay physically active (2.5 hours each week of moderate exercise) ☐ Don't smoke or use chewing tobacco ☐ Stay away from places where people usually smoke ☐ Don't let people smoke in your house or car Smoking cigarettes or using tobacco hurts nearly every organ in the body, especially your lungs and heart. It can also cause new cancers.	• What are some exercises I can do to stay physically active? • Are medications to help me quit smoking an option? If so, which ones? How long will I be on them? What are the side effects of the medications? • Where can I go for counseling or a support group to quit smoking?
New cancers	**Questions to ask your doctor and your notes**
New cancers can develop because you've had chemotherapy and/or radiation, TBI and have a history of GVHD. You need to have screenings at least 1 time every year for: ☐ Breast cancer (**mammography** every 1 to 2 years starting at age 25) ☐ Cervical cancer ☐ Colorectal cancer (starting at age 50 or earlier if you have a family history of colorectal cancer) ☐ Skin cancer	• What is my risk for getting new cancers? • How can I lower my risk of getting new cancers? • How do I do a self-exam of my skin? How often? What should I be looking for? • Would I benefit from annual skin exams?

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YOUR CARE TEAM INFORMATION	
Transplant doctor:	
Phone:	
Primary care doctor:	
Clinic name:	**Phone:**
Oncology (cancer) doctor:	
Clinic name:	**Phone:**
Ophthalmologist (eye specialist):	
Clinic name:	**Phone:**
OB/GYN (women's health specialist):	
Clinic name:	**Phone:**
Physical Therapist:	
Clinic name:	**Phone:**
Dentist:	
Clinic name:	**Phone:**
Other doctor:	
Clinic name:	**Phone:**
Other doctor:	
Clinic name:	**Phone:**
Other doctor:	
Clinic name:	**Phone:**

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YOUR TREATMENT NOTES

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Folder Cover

Individualized Care Plans for HCT Survivors

Study funding provided by the Patient Centered Outcomes Research Institute (PCORI) and sponsored by Be the Match®. This study is conducted by the Center for International Blood and Marrow Transplant Research (CIBMTR) Resource for Clinical Investigation in Blood and Marrow Transplant (RCI BMT).

Your study materials

Inside Left Panel

Congratulations on the one-year anniversary of your blood and marrow transplant (transplant), also known as HCT. Thank you for joining the Individualized Care Plans for HCT Survivors study. This folder contains your study materials:

- Your personalized care plan
- Glossary of terms
- Actions you can take to get the most out of your care plan
- How to get answers to your questions

A survivorship care plan includes a summary of your transplant treatment and plan for follow-up care. You and your doctors can use this information to make decisions together about your care. Transplant follow-up care is important to protecting your heath, even many years after transplant.

Your transplant center reviewed the information in this care plan. For this study, treatments or issues that you might have had before transplant are not included in the care plan. Please contact your transplant center or hematologist/oncologist (cancer doctor) for your questions about treatment before transplant.

We will use your feedback to improve HCT survivorship care plans in the future.

Sincerely,

Elizabeth A. Murphy	*K. Scott Baker*	*Navneet S. Majhail*
Elizabeth Murphy, RN, EdD	K. Scott Baker, MD, MS	Navneet Majhail, MD, MS
Principal Investigator	Co-Principal Investigator	Co-Principal Investigator

Inside Right Panel

Glossary

Bone density scan — An imaging (picture) test that looks for abnormal (or unhealthy) areas in your bones. For this test, you are given a small amount of a fluid in your arm. The fluid is a radioactive contrast material (like a dye) that settles in abnormal areas of the bones. The dye can then be seen in pictures. When bone density is low, your bones become more porous (full of holes) and brittle. When this happens, you have a higher risk of breaking them.

Cytomegalovirus (CMV) — A type of herpes virus that can cause infections (for example, pneumonia).

Endocrine organs — Endocrine organs release hormones into your blood to manage body functions like your mood and growth. Endocrine organs include the thyroid, pituitary, and pancreas glands.

Fasciitis — Inflammation (redness and swelling) of the connective tissue that surrounds muscles, blood vessels, and nerves. Often patient get fasciitis and hardening of the skin (see **Scleroderma**) at the same time.

Fertility — A person's ability to have children

Gastrointestinal (GI) tract — Also called the digestive tract. It is made up of body organs that process the food you eat. The GI tract includes the throat, stomach, and intestines.

Graft-Versus-Host Disease (GVHD) — A post-transplant condition where the donor cells attack the patient's tissues or organs.

HDL cholesterol — High-density lipoprotein or HDL is known as "good" cholesterol because it helps to remove "bad" cholesterol (LDL) and keep your blood vessels healthy (see **LDL**).

Immunosuppressant drugs — Immunosuppressant drugs work to lower the strength of your immune system. The main use of these drugs is to lower the body's ability to reject the transplanted bone marrow, cord blood or peripheral blood stem cells. Immunosuppressant drugs are usually given to treat GVHD.

Kidney disease — When your kidneys don't properly filter toxins (or poisons) and waste products from your blood.

Kidney filtration levels test — Measures how much liquid flows through your kidneys. This test is used to see if you have chronic kidney disease.

LDL cholesterol — Low-density lipoprotein or LDL is known as "bad" cholesterol. When you have too much LDL is your blood, it can form a thick, hard deposit. If a clot forms and blocks an artery, you might have a heart attack or stroke.

Mammography — An imaging (picture) test to see if you have breast cancer.

Meningitis — Inflammation of the membranes covering your brain and spinal cord. This is caused by viruses, fungi or bacteria.

Myopathy — Muscle disease and weakness. Steroids are used to treat chronic GVHD, but might result in muscle weakness, especially in your lower body (for example, your legs and feet).

Osteopenia — Thinning of your bone tissue. Bones are weak with Osteopenia, but not as weak as with Osteoporosis. Patients develop Osteopenia before Osteoporosis.

Osteoporosis — A lot of thinning of your bone tissue, causing very weak bones. Osteoporosis can cause pain and lead to broken bones.

Oral cancer — Cancer of the mouth.

Pneumonia — Inflammation of the lungs caused by viruses, fungi, or bacteria.

Pulmonary function tests — A group of tests to measure how well the lungs are working.

Range of motion — A test to find out if a joint (such as elbow, hip, wrist) can move properly and in all normal directions.

Scleroderma — When your skin becomes hard, thick, and tight. This can lead to weak muscles, stiff joints or pain in your joints.

Thyroid — A gland that controls your body's metabolism. Metabolism is how quickly your body uses energy from the food you eat.

Fold-in Panel

Take action

- ☐ Schedule twelve-month check-up appointments with your transplant doctor or your hematologist/oncologist.
- ☐ Review the tests, procedures and questions to ask your doctor listed in the care plan inside.
- ☐ Write down questions or issues you'd like to discuss at your appointments.

- Ask your doctor if there are other recommendations unique to your situation.
- Bring this care plan to all of your appointments.
- At your appointment, ask your doctor if you need to schedule appointments with other health care providers (for example, eye doctor, dentist, physical therapist, OB/GYN, counselor or other specialists).
- You might have more than 1 doctor. Talk with your doctors and encourage them to speak with each other. This will help you know who to call when you have new symptoms or to schedule checkup appointments.

Share with your doctor

- Review this guide with them at your next appointment.
- Ask them to make a copy for your medical record.

For questions or more information

You might have questions about your care plan. For answers to these questions, contact your transplant center. The name and phone number for your transplant center are listed on the care plan inside.

You might have questions about this study. For answers to these questions, contact the Investigator at your transplant center. This information is provided in your consent form and the patient information sheet. You can also contact the Center for International Blood and Marrow Transplant Research (CIBMTR) study team by:

Phone: 1-800-526-7809 Ext. 4368 (toll-free)

E-mail: SCP_SRGTeam@nmdp.org