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ORIGINAL REPORT

Randomized Clinical Trial of Telephone-Administered Cognitive-Behavioral Therapy to Reduce Post-Traumatic Stress Disorder and Distress Symptoms After Hematopoietic Stem-Cell Transplantation

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Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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ABSTRACT

Purpose
A significant number of survivors of hematopoietic stem-cell transplantation (HSCT) report enduring adverse effects of treatment, including illness-related post-traumatic stress disorder (PTSD) symptoms and general distress. We report results of a randomized clinical trial that tested the effects of a 10-session, telephone-administered cognitive-behavioral therapy (CBT) intervention on PTSD, depression, and distress symptoms.

Methods
Survivors who had undergone HSCT 1 to 3 years earlier (N = 408) were assessed for study eligibility. Those who met study eligibility criteria (n = 89) completed a baseline assessment that included a clinical interview and self-report measures of PTSD symptoms (the primary outcome) and depression and general distress (the secondary outcomes). Next, they were randomly assigned to CBT or an assessment-only condition. Survivors in the CBT group completed 10 individual telephone-based CBT sessions (T-CBT) that included strategies to reduce PTSD symptoms, depression, and general distress. Follow-up assessments occurred at 6, 9, and 12 months after the baseline assessment.

Results
Linear mixed-model analyses revealed that, compared with HSCT survivors in the assessment-only condition, survivors who completed T-CBT reported fewer illness-related PTSD symptoms, including less avoidance ($P < .001$) and fewer intrusive thoughts ($P < .05$) as well as less general distress and fewer depressive symptoms ($P < .05$) even after controlling for potential demographic and medical covariates. These results were consistent across the three follow-up assessments.

Conclusion
A brief, telephone-administered CBT intervention developed for HSCT survivors is an efficacious treatment for reducing illness-related PTSD symptoms and general distress.

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INTRODUCTION

Hematopoietic stem-cell transplantation (HSCT) is an increasingly common treatment for hematologic and lymphoid cancers and nonmalignant diseases.[1] Many survivors of HSCT experience long-term medical and psychological adjustment problems, such as post-traumatic stress disorder (PTSD) symptoms.[1-2] These symptoms include intrusive thoughts, avoiding reminders of illness experiences, and physiologic arousal on exposure to illness-related cues.[3] Research suggests that as many as 41% of survivors of HSCT experience persistent PTSD symptoms up to 10 years post transplantation[3-8] and that general distress and depressive symptoms affect up to 40% of survivors.[2]

Cognitive-behavioral therapy (CBT) has been found to reduce cancer-related adjustment problems.[9-12] For example, a 10-session cognitive-behavioral intervention reduced depression among patients with early-stage breast cancer.[13] With noncancer trauma populations, including military veterans and survivors of sexual assault, CBT has reduced PTSD symptoms and psychiatric comorbidities, such as depression.[14-15]

On the basis of these prior CBT trials[11,13,15-16] and our clinical experience with patients who have cancer and who survived HSCT,[17] we developed a telephone-administered CBT (T-CBT) intervention

for survivors of HSCT that focused on the maladaptive emotional reactions to illness and transplantation. We hypothesized that this intervention would reduce symptoms of illness-related PTSD (the primary study outcome), general distress, and depression (the secondary study outcomes) in survivors of HSCT. We tested this hypothesis by comparing psychologic outcomes of a T-CBT group to those of an assessment-only control group. Treatment effects were evidenced either by a significant study group main effect or by a significant time-by–study group interaction. On the basis of unpublished pilot data for this study, a main effect for treatment group was anticipated for the continuous measure of PTSD, as the pilot data indicated that, even in the absence of treatment, a decline in PTSD symptoms occurred over time. Because no pilot data were obtained for the categoric measure of PTSD or for the measures of distress and depression, there were no clear a priori hypotheses with regard to a significant main effect for treatment condition or an interaction between time and treatment. Finally, we explored the influence of demographic and medical factors on the outcomes.

METHODS

Participants

Potential participants were recruited from Memorial Sloan-Kettering Cancer Center, the Mount Sinai School of Medicine, and Hackensack University Medical Center. Inclusion requirements were HSCT performed 12 to 36 months before study enrollment, English fluency, 18 years of age or older, and significant distress as indicated by at least one of the following three criteria: probable illness-related PTSD on the PTSD Checklist-Civilian Version (PCL-C) by using the three- or four-symptom cluster criteria;[8,18] subclinical PTSD symptoms as indicated by scores one or more standard deviations greater than the PCL-C mean; or general distress with some PTSD symptoms as indicated by scores exceeding the clinical cutoff on any two subscales of the Brief Symptom Inventory[19] (BSI) or the BSI Global Severity Index and, according to either PCL-C scoring method, scores exceeding the cutoff for at least one PTSD symptom cluster.

Survivors were excluded from study participation if they were currently awaiting another transplantation or receiving treatment for disease relapse; had severe cognitive impairment assessed with the six-item Mini-Mental State Exam;[20] experienced active psychosis assessed with six items from the Psychotic Symptoms module of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders fourth edition text revision (DSM-IV-TR);[21] reported suicidal ideation assessed with one item from the Beck Depression Inventory[22] and one from the BSI;[19,23] or had substance dependence assessed with the four-item Rapid Alcohol Problems Screen-4[24] and the two-item Conjoint Screen[25] for alcohol and other drug problems.

Procedures

After approval by the institutional review boards, oncologists or their representatives identified potentially eligible survivors of HSCT. Each survivor was mailed a letter and brochure describing the study, a consent form, and psychosocial questionnaires. Trained research assistants obtained verbal consent from survivors via telephone. Participants first completed a telephone screening interview that assessed sociodemographics and symptoms of PTSD, general distress, and depression. Next, those who met study eligibility criteria completed a baseline telephone interview that included a PTSD diagnostic interview and measures of PTSD, general distress, and depressive symptoms. Computerized random assignment occurred approximately 1 week postbaseline. Interviewers were blinded to participant group assignment.

Intervention

The 10-session manualized T-CBT intervention was delivered during a period of 10 to 16 weeks. The first session was approximately 90 minutes in duration, and sessions 2 to 10 were approximately 60 minutes. Interventionists were postdoctoral psychology research fellows who completed 12 hours of training with an expert in CBT for PTSD and study team members. They were supervised individually and as a group by senior CBT clinicians throughout the study. The intervention manual from a previous study[17] was revised, and participants received a workbook to accompany the telephone sessions. The intervention included education regarding illness-related PTSD symptoms and CBT (eg, characterizing PTSD symptoms in cancer and other trauma populations and ways in which CBT can reduce these symptoms), self monitoring and alteration of maladaptive beliefs,[26] guided exposure to cues associated with PTSD symptoms,[27] enhancement of social support through training in communication skills,[28-30] and relaxation training[31] (study manual available from K.D.). Each component focused on distress related to the participant's disease and transplantation. The percentage of participants who completed each session ranged from 92% for sessions 1 and 2 to 79% for sessions 7 to 10. The mean number of sessions attended by the participants was 8.36 (standard deviation [SD], 3.27).

Follow-Up

Baseline measures were readministered during three telephone follow-up interviews. Follow-ups occurred approximately 6 months (mean, 5.71 months; SD, 1.97), 9 months (mean, 8.57 months; SD, 2.21), and 12 months after the baseline assessment (mean, 12.16 months; SD, 1.86).

Measures

PCL-C. The PCL-C[18] is a measure of illness-related PTSD symptoms previously used with survivors of HSCT.[3] The PCL-C yields a total score and subscale scores for intrusive thoughts, avoidance, numbing, and hyperarousal.[8]

BSI. The BSI[19] is a questionnaire that assesses general psychological distress. Because general distress and depressive symptoms often co-occur with PTSD,[7] the Global Severity Index (GSI) and the depression subscale were used in this study.

Clinician-Administered PTSD Scale for DSM-IV. The Clinician-Administered PTSD Scale for DSM-IV (CAPS)[32] is a structured diagnostic interview that is based on DSM-IV criteria for PTSD. The CAPS is sensitive to short-term changes in PTSD symptoms.[32-33]

Sociodemographic and medical variables. Participants reported their sociodemographic data, and medical information, such as the type of transplantation and graft-versus-host disease (GVHD), was obtained from chart review at screening and approximately 6 to 12 months postbaseline.

Statistical Analysis

Before undertaking the main analyses, all continuous explanatory and outcome variables were assessed for normality and the presence of outliers. The primary analyses focused on PTSD symptoms by using a linear mixed-model repeated measures approach for the continuous PCL-C scores (SAS Proc Mixed, version 9.2; SAS Institute, Cary, NC) and a Generalized Estimating Equations (GEE) model for the binary PTSD diagnosis that is based on the CAPS (SAS Proc Genmod, version 9.2; SAS Institute). Because both the linear mixed-model and GEE procedures utilize all the data each participant provided (even if the participant was a study dropout), an intent-to-treat (ITT) framework was implemented. For each outcome, the model included the main effects for time, the distress criteria for study entry, study group, and the time-by–study group interaction. Two-tailed tests of significance were employed. Treatment effects were evidenced either by a significant study group main effect or by a significant interaction between time and study group.

Two secondary outcomes (BSI Global Distress and BSI Depression) were also evaluated by using the same ITT approach. Probabilities for these four outcomes were Sidak adjusted for correlated multiple outcomes (average correlation, 0.56; adjusted probability for significance, 0.0280). In additional secondary analyses, covariates were examined on the basis of correlations of the sociodemographic and medical variables with each outcome.

RESULTS

Demographic and Medical Characteristics

Of the 1,434 survivors approached regarding the study, 452 consented to participate, and 408 of these individuals completed the

screening assessment to determine eligibility (Fig 1). Common reasons for inability to complete screening were inability to contact the participant (n = 25) and participant refusal (n = 6). Ten participants were not screened because the study ended before they could be scheduled. None of the variables that had a sufficient amount of nonmissing responses (eg, age, ethnicity, sex, time elapsed since treatment) were significant predictors of screening completion by using logistic regression.

Of the 408 participants screened, 89 (21.8%) met study distress criteria and were randomly assigned. Of these 89 participants,

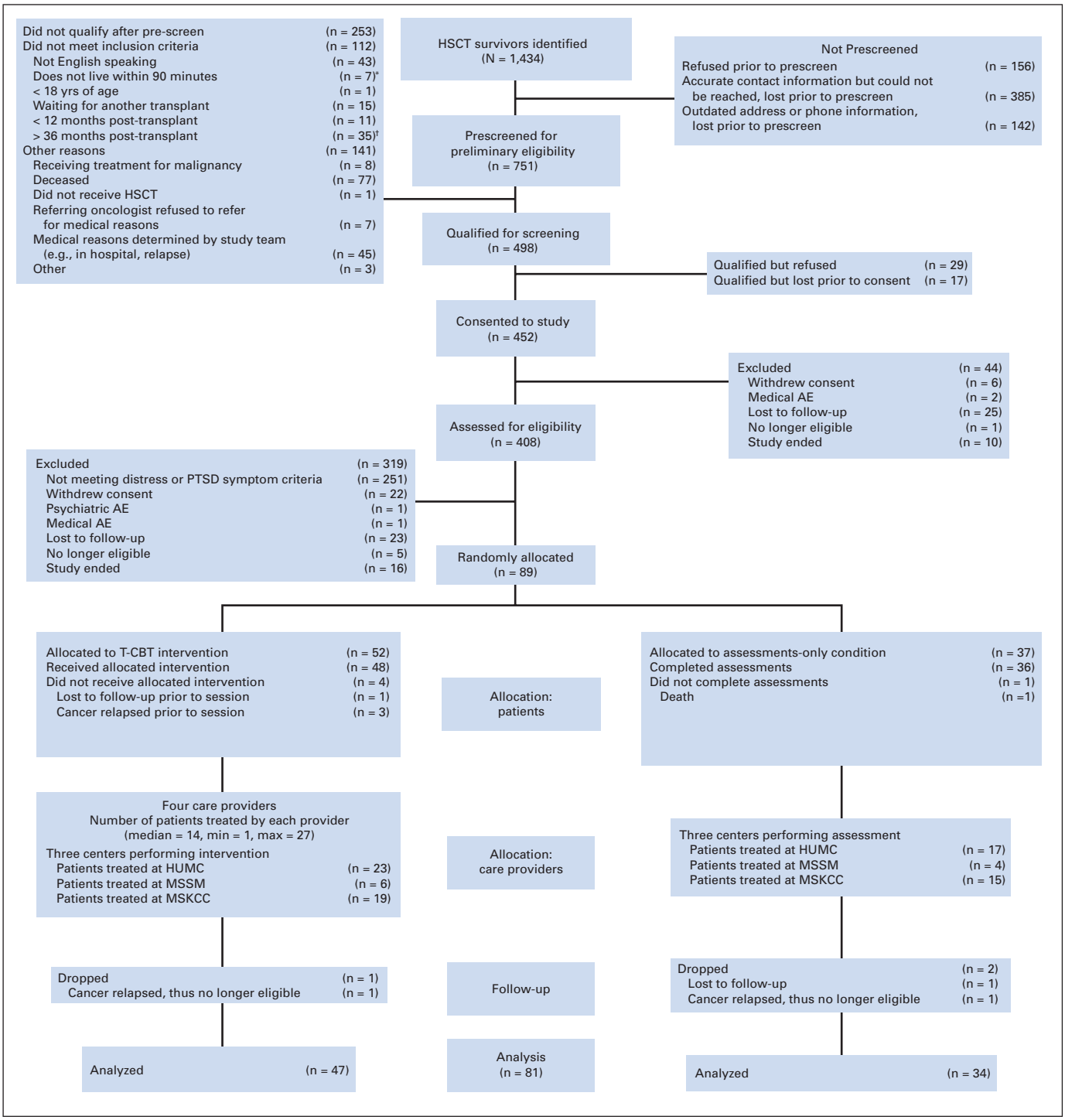

Fig 1. CONSORT: telephone-based cognitive-behavioral therapy (T-CBT) trial participant flow. (*)Inclusion criteria were modified during the study to include individuals who lived beyond 90 minutes of a site. However, by the time criteria were modified to include these seven individuals, they were ineligible due to being longer than 36 months post-transplant. (†)Not including seven individuals referred to above. HSCT, hematopoietic stem-cell transplantation; PTSD, post-traumatic stress disorder; AE, adverse event; HUMC, Hackensack University Medical Center; MSSM, Mount Sinai School of Medicine; MSKCC, Memorial Sloan-Kettering Cancer Center.

Table 1. Baseline Sociodemographic and Clinical Characteristics

Characteristic	T-CBT Group (n = 47)		Assessment-Only Group (n = 34)	
	No. of Participants	%	No. of Participants	%
Age, years				
Mean	52.19		49.38	
Standard deviation	10.5		13.41	
Range	27-71		19-74	
Sex				
Female	19	40.4	22	64.7
Male	28	59.6	12	35.3
Ethnicity				
African American	2	4.3	0	0
White	39	83.0	27	79.4
Hispanic	3	6.4	3	8.8
West Indian	0	0	2	5.9
Other	3	6.4	1	2.9
Marital status				
Married or equivalent	36	76.6	20	58.8
Never married	6	12.8	8	23.5
Separated	1	2.1	2	5.9
Divorced	1	2.1	3	8.8
Widowed	1	2.1	1	2.9
Engaged to be married	2	4.3	0	0
Education				
High school or less	9	19.1	8	23.5
Some college	8	17.0	8	23.5
College/graduate degree	30	63.8	18	52.9
Income, $				
Less than 19,999	5	10.6	3	8.8
20,000-39,999	2	4.3	2	5.9
40,000-59,999	8	17.0	7	20.6
60,000-79,999	6	12.8	5	14.7
Greater than 80,000	25	53.2	14	41.2
Missing	1	2.1	3	8.8
Time since transplantation, years				
Mean	23.38		22.08	
Standard deviation	7.41		6.69	
Range	13-36		14-38	
Disease status				
Free of disease	25	53.2	19	55.9
Alive with disease	14	29.8	6	17.6
Missing	8	17.0	9	26.5
Transplantation type				
Autologous	28	59.6	12	35.3
Allogeneic	17	36.2	18	52.9
Missing	2	4.3	4	11.8
GVHD				
Chronic GVHD	2	4.3	3	8.8
History of acute GVHD	3	6.4	7	20.6
Hospitalizations after discharge, months				
0	18	38.3	13	38.2
1-2	15	31.9	9	26.5
3-4	6	12.8	2	5.9
More than 4	1	2.1	2	5.9
Missing	7	14.9	8	23.5
Disease type				
Non-Hodgkin's lymphoma	7	14.9	7	20.6
Hodgkin's lymphoma	3	6.4	5	14.7
Acute and chronic myeloid leukemia	10	21.3	5	14.7
Acute and chronic lymphoid leukemia	0	0	4	11.8
Myelodysplastic syndrome or myeloproliferative disease	5	10.6	4	11.8
Multiple myeloma or amyloidosis	18	38.3	3	8.8
Other	0	0	1	2.9
Missing	4	8.5	5	14.7

Abbreviations: T-CBT, telephone-based cognitive-behavioral therapy; GVHD, graft-versus-host disease.

two were lost to follow-up, and six withdrew because of serious adverse events and/or disease relapse. This resulted in a final sample of 81 participants.

Table 1 presents descriptive statistics by group assignment. At study entry, 15 (19%) of the 81 participants met criteria for a three-symptom cluster diagnosis of PTSD, and 58 (72%) met criteria for a four-symptom cluster diagnosis of PTSD. Almost all participants (n = 78 [96%]) met criteria for general distress with some PTSD symptoms.

Primary Outcome: Post-Traumatic Stress Disorder Symptoms—Total Score

A main effect for treatment group was anticipated and, indeed, the ITT analysis of post-traumatic stress symptoms (ie, PCL-C) yielded a significant ($t(80) = 2.37$; $P = .0201$) main effect for study group in favor of T-CBT ($M_{\text{Control}} = 33.03$; 95% CI, 29.87 to 36.18; $M_{T\text{-CBT}} = 28.34$; 95% CI, 25.04 to 31.62). Mean scores for this primary outcome can be found in Table 2.

Because the two groups differed significantly on the total PCL-C score and because there is evidence that the PCL-C scale consists of four factors (intrusive thoughts, avoidance, hyperarousal, numbing),[8] follow-up analyses were conducted to examine intervention effects on these four symptom clusters.

Post-Traumatic Stress Disorder Symptoms: Cluster Subscales

The ITT analysis of intrusive thoughts yielded a significant ($t(80) = 2.60$; $P = .011$) main effect for study group in favor of T-CBT ($M_{\text{Control}} = 10.36$; 95% CI, 9.10 to 11.62; $M_{T\text{-CBT}} = 8.62$; 95% CI, 7.77 to 9.48). The ITT analysis of avoidance also yielded a significant ($t(80) = 3.95$; $P < .001$) main effect for study group again in favor of T-CBT ($M_{\text{Control}} = 4.13$; 95% CI, 3.60 to 4.65; $M_{T\text{-CBT}} = 2.98$; 95% CI, 2.59 to 3.37). There were, however, no treatment effects for the numbing or hyperarousal subscales.

Primary Outcome: PTSD Diagnosis

Next, we conducted an ITT GEE analysis of the PTSD diagnosis that was based on the CAPS. There was no a priori reason to expect either a significant study group main effect or a time-by–study group interaction. There was a significant ($z = -2.22$; $P = .027$) time-by–study group effect. To understand this interaction, group differences were examined at the beginning and end of the assessment period (ie, at baseline and 12 months postbaseline). As expected, there were no significant ($z = 1.10$; $P = .27$) study group differences at baseline. However, at the 12-month follow-up, there was a significant ($z = -2.06$; $P = .04$) difference in the log odds of not being diagnosed with PTSD (odds ratio]OR], 0.07; 95% CI, 0.006 to 0.88) in favor of the T-CBT group. Mean log odds scores for each group across time are listed in Table 2.

Secondary Outcome: BSI General Distress

The ITT analysis of BSI Global Distress yielded a significant ($F(4,80) = 4.05$; $P = .005$) time-by–study group interaction (Table 3). The interaction means displayed in Figure 2 show a steady decline in general distress for the T-CBT group, whereas the mean scores for the control group show some decline from screening to baseline but remain relatively stable over subsequent assessments.

Secondary Outcome: BSI Depressive Symptoms

The ITT analysis yielded a significant ($F(4,208) = 2.89$; $P = .023$) time by study group interaction on BSI Depression (Table 3). The means displayed in Figure 3 follow the same pattern as that found for general distress. Notably, the CIs for mean depressive symptoms at the three follow-up assessments for the T-CBT group contained zero, which indicated that they did not differ significantly from zero.

Covariate Analyses: PTSD

In covariate analyses, we examined the effects of the sociodemographic and medical measures reported in Table 1. None of these covariates predicted total PCL-C score. However, in the GEE analysis of the PTSD diagnosis that was based on the CAPS, the time that had elapsed since HSCT was significant ($z = -2.36$; $P = .019$). The shorter the time since transplantation completion was, the greater the likelihood that the survivor was diagnosed with PTSD (OR, 1.9; 95% CI, 1.02 to 1.17). Survivors declared disease free were marginally ($z = 1.80$; $P = .07$) more likely to be diagnosed with PTSD (OR, 4.58; 95% CI, 0.88 to 23.69). After analysis was adjusted for these covariates, the time-by–study group interaction continued to be significant ($z = -2.46$; $P = .014$). This interaction was examined through analysis of treatment effects at baseline and the last assessment. Once more, there

Table 2. Study Group Means and 95% CIs for PTSD Symptoms

	T-CBT Group		Assessment-Only Group	
Outcome	Mean	95% CI	Mean	95% CI
Total PCL-C				
Screening	34.01	30.79 to 37.24	38.23	35.27 to 41.20
Baseline	32.05	28.60 to 35.50	33.97	30.18 to 37.76
6 months postbaseline	25.38	21.69 to 29.07	32.05	27.18 to 36.93
9 months postbaseline	24.63	21.08 to 28.18	31.99	27.42 to 36.56
12 months postbaseline	24.00	19.20 to 28.01	30.89	26.33 to 35.45
PTSD diagnosis				
Baseline	−1.25	−2.00 to −0.50	−1.97	−3.00 to −0.94
6 months postbaseline	−2.31	−3.14 to −1.48	−1.92	−2.62 to −0.98
9 months postbaseline	−3.37	−4.73 to −2.01	−1.87	−2.76 to −0.98
12 months postbaseline	−4.42	−6.43 to −2.42	−1.82	−3.23 to −0.42

Abbreviations: PTSD, post-traumatic stress disorder; T-CBT, telephone-based cognitive behavioral therapy; PCL-C, PTSD Checklist-Civilian Version.

Table 3. Time-by–Study Group Interaction: Means and 95% CIs for General Distress and Depressive Symptoms

Outcome	T-CBT Group		Assessment-Only Group	
	Mean	95% CI	Mean	95% CI
Global BSI distress				
Screening	40.87	32.56 to 49.18	47.56	40.62 to 54.49
Baseline	34.87	26.67 to 43.07	35.82	25.43 to 46.22
6 months postbaseline	21.36	12.56 to 30.17	38.84	25.73 to 51.96
9 months postbaseline	17.90	9.11 to 26.69	37.71	27.29 to 48.13
12 months postbaseline	16.93	7.88 to 25.98	38.08	26.66 to 49.49
BSI depression				
Screening	3.93	2.00 to 5.86	5.30	3.76 to 6.84
Baseline	3.62	1.70 to 5.54	3.81	2.13 to 5.49
6 months postbaseline	1.80	−0.08 to 3.69	4.28	2.23 to 6.32
9 months postbaseline	1.30	−0.56 to 3.14	4.20	2.29 to 6.12
12 months postbaseline	1.34	−0.54 to 3.21	3.95	1.67 to 6.23

Abbreviations: T-CBT, telephone-based cognitive-behavioral therapy; BSI, Brief Symptom Inventory.

was no significant baseline difference ($z = 1.02$; $P = .308$) between the two groups in PTSD diagnosis. By study end, however, those in T-CBT were significantly ($z = -2.69$; $P = .007$) less likely to be diagnosed with PTSD (OR, 0.046; 95% CI, 0.004 to 0.43).

Covariate Analyses: General Distress

Two significant covariates predicted general distress on the BSI Global Distress scale. Married survivors reported significantly lower general distress ($t(78) = -3.04$; $P = .003$), and less well-educated survivors reported significantly greater general distress ($t(78) = -2.44$; $P = .017$). The time-by–study group interaction continued to be significant ($F(4,78) = 4.34$; $P = .003$). Table 4 contains the covariate-adjusted means. Moreover, the pattern of change for those in T-CBT continued to show a temporal decline, whereas average scores for control condition survivors remained relatively constant.

Covariate Analyses: Depressive Symptoms

Marital status was a significant ($t(63) = -2.44$; $P = .018$) predictor of BSI depression. Married survivors reported significantly fewer depressive symptoms. Number of hospitalizations was marginally significant ($t(63) = 1.93$; $P = .058$). As the number of hospitalizations increased, depressive symptoms also increased. The time-by–study group interaction continued to be significant ($F(4,177) = 2.43$; $P = .049$) after analysis was controlled for these variables. Table 4 summarizes the adjusted means and shows a decline in depressive symptoms for the T-CBT group. In contrast, survivors in the assessment-only condition demonstrated an initial decline (a nonsignificant difference from screening to baseline) and a subsequent increase in depressive symptoms at the third, fourth, and final assessments.

DISCUSSION

Survivors who participated in the 10-session T-CBT intervention experienced fewer PTSD symptoms, including fewer illness-related intrusive thoughts and less avoidance across all follow-up assessments. T-CBT participants also were less likely to meet diagnostic criteria for PTSD at the final assessment and showed lower general distress and depressive symptoms at all follow-up assessments. Previous

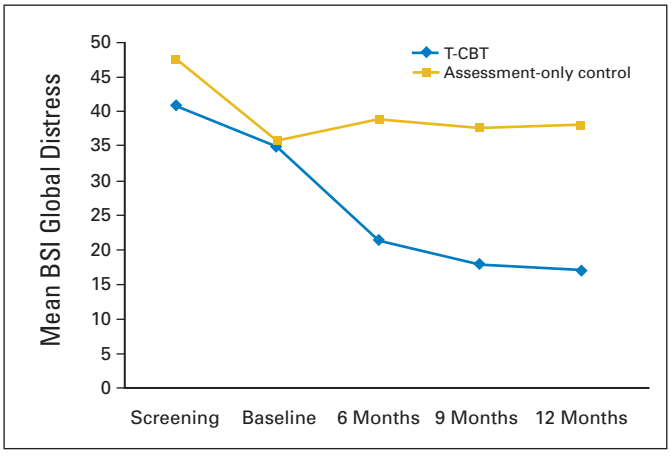

Fig 2. Changes in global distress by study condition. BSI, Brief Symptom Inventory; T-CBT, telephone-based cognitive-behavioral therapy.

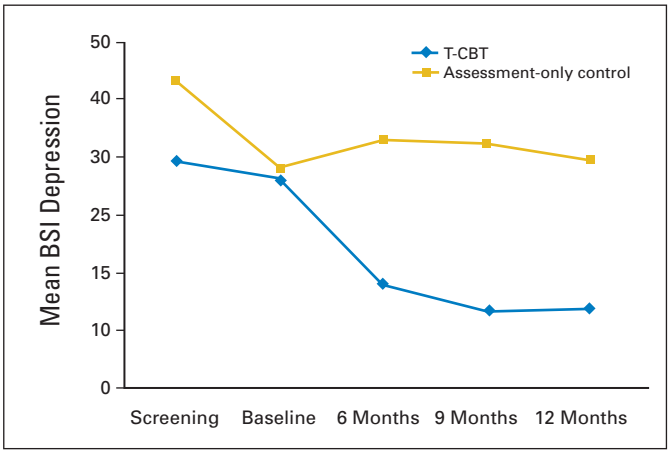

Fig 3. Changes in depressive symptoms by study condition. BSI, Brief Symptom Inventory; T-CBT, telephone-based cognitive-behavioral therapy.

Table 4. Time-by–Study Group Interaction: Covariate-Adjusted Means and 95% CIs for General Distress and Depressive Symptoms

Outcome	T-CBT Group		Assessment-Only Group	
	Mean	95% CI	Mean	95% CI
Global BSI distress				
Screening	46.80	36.47 to 57.13	48.52	39.41 to 57.62
Baseline	40.97	30.70 to 51.25	36.80	24.97 to 48.64
6 months postbaseline	27.74	16.83 to 38.65	40.54	26.45 to 54.63
9 months postbaseline	24.56	9.11 to 26.69	40.62	28.18 to 53.06
12 months postbaseline	23.41	12.01 to 34.82	39.61	26.82 to 52.41
BSI depression				
Screening	6.39	4.82 to 7.96	7.11	5.30 to 8.92
Baseline	6.08	4.55 to 7.61	5.70	3.53 to 7.87
6 months postbaseline	4.62	3.06 to 6.18	6.47	3.76 to 9.18
9 months postbaseline	4.31	2.70 to 5.93	6.43	3.96 to 8.89
12 months postbaseline	4.47	2.74 to 6.19	6.20	3.92 to 8.49

Abbreviations: T-CBT, telephone-based cognitive-behavioral therapy; BSI, Brief Symptom Inventory.

in-person CBT interventions have reduced general distress during cancer treatment,[12,34] whereas T-CBT is the first intervention to reduce illness-specific PTSD during the early phase of HSCT survivorship. Several components of T-CBT (ie, education regarding PTSD and CBT, relaxation training, guided exposure to cues associated with PTSD responses, and changing maladaptive beliefs) targeted PTSD symptoms. The goal of T-CBT was to reduce illness-related fears of the survivors and to facilitate cognitive processing of their transplantation experiences (ie, incorporation of the experiences into their worldviews). As depressive symptoms and general distress are often comorbid with PTSD symptoms and were part of the study entry criteria, these symptoms were addressed through training in methods of accessing social support and challenging negative thoughts.

Although the T-CBT intervention reduced total PTSD symptom scores, more detailed analyses indicated that T-CBT was effective for intrusive thoughts and avoidance but not for numbing and hyperarousal. This finding may be because, although avoidance and intrusive thoughts were targeted via exposure exercises, feelings of numbness or emotional detachment from others were not directly addressed. In addition, relaxation and challenging maladaptive beliefs did not reduce hyperarousal associated with life-threatening illness. Additional intervention development is needed to address these symptoms.

Relations of sociodemographic and medical factors to study outcomes also were explored. Shorter time since transplantation was associated with a greater likelihood of being diagnosed with PTSD (on the basis of the CAPS) during this early phase of survivorship, whereas total self-reported PTSD symptoms were not associated with any sociodemographic or medical variables. In addition, being married was associated with less general distress and fewer depressive symptoms, and more education was associated with less general distress, consistent with prior research.[35-37]

Study limitations include the under representation of ethnic minorities and exclusion of those who lacked English fluency. None of the variables tested (age, ethnicity, sex, time elapsed since treatment) were predictors of screening completion by using logistic regression. It is possible that level of distress may have been associated with screening completion, which could not be tested in this study. However, levels of distress among those who completed the screening interview did not differ from those found in prior research with HSCT survivors.[38] In addition, the study entry criteria involved a combination of sex-keyed, nonpatient, BSI clinical cutoffs[19] and PTSD symptoms for which normative data were unavailable. Finally, use of an assessment-only control condition did not control for attention provided to survivors. Future research should compare T-CBT for HSCT survivors to alternatives such as supportive therapy, which can control for time and attention and which is frequently used in CBT trials with other populations.[39] T-CBT also needs to be modified for culturally diverse populations and its cost effectiveness should be examined.

This study informs clinical care by showing that a novel, telephone-administered CBT intervention can reduce illness-related PTSD, general distress, and depressive symptoms among HSCT survivors. The rigorous methodology (eg, random assignment, blind follow-ups, manualized treatment, a well-defined population who met criteria for distress) enhances confidence in the findings. Finally, this telephone intervention may be readily disseminated to geographically dispersed survivors and those with physical impairments that limit their abilities to take advantage of in-person treatments. In addition, telephone-based counseling may be preferable for some survivors with PTSD who avoid contact with the hospital because of the anxiety it provokes. The next step is to disseminate this intervention and to increase awareness of PTSD symptoms and their treatment among HSCT survivors, their families, and their health care team.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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REFERENCES

1. Copelan EA: Hematopoietic stem-cell transplantation. N Engl J Med 354:1813-1826, 2006

2. Mosher CE, Redd WH, Rini CM, et al: Physical, psychological, and social sequelae following hematopoietic stem cell transplantation: A review of the literature. Psychooncology 18:113-127, 2009

3. Smith MY, Redd W, DuHamel K, et al: Validation of the PTSD Checklist-Civilian Version in survivors of bone marrow transplantation. J Trauma Stress 12:485-499, 1999

4. Cordova MJ, Andrykowski MA: Frequency and correlates of PTSD after bone marrow transplant. Presented at the 20th Annual Meeting of the Society of Behavioral Medicine, San Diego, CA, March 3-6, 1999

5. Jacobsen PB, Widows MR, Hann DM, et al: Posttraumatic stress disorder symptoms after bone marrow transplantation for breast cancer. Psychosom Med 60:366-371, 1998

6. Jacobsen PB, Sadler IJ, Booth-Jones M, et al: Predictors of posttraumatic stress disorder symptomatology following bone marrow transplantation for cancer. J Consult Clin Psychol 70:235-240, 2002

7. Mundy EA, Blanchard EB, Cirenza E, et al: Posttraumatic stress disorder in breast cancer patients following autologous bone marrow transplantation or conventional cancer treatments. Behav Res Ther 38:1015-1027, 2000

8. DuHamel KN, Ostroff J, Ashman T, et al: Construct validity of the posttraumatic stress disorder checklist in cancer survivors: Analyses based on two samples. Psychol Assess 16:255-266, 2004

9. Fawzy FI, Fawzy NW, Arndt LA, et al: Critical review of psychosocial interventions in cancer care. Arch Gen Psychiatry 52:100-113, 1995

10. Cwikel J, Behar L, Rabson-Hare J: A comparison of a vote count and a meta-analysis review of intervention research with adult cancer patients. Res Soc Work Pract 10:139-158, 2000

11. Moorey S, Greer S, Bliss J, et al: A comparison of adjuvant psychological therapy and supportive counselling in patients with cancer. Psychooncology 7:218-228, 1998

12. Tatrow K, Montgomery GH: Cognitive behavioral therapy techniques for distress and pain in breast cancer patients: A meta-analysis. J Behav Med 29:17-27, 2006

13. Antoni MH, Lehman JM, Kilbourn KM, et al: Cognitive-behavioral stress management intervention decreases the prevalence of depression and enhances benefit finding among women under treatment for early-stage breast cancer. Health Psychol 20:20-32, 2001

14. PTSD Treatment Guidelines Task Force: Guidelines for treatment of PTSD. J Trauma Stress 13:539-588, 2000

15. Foa EB, Hearst-Ikeda D, Perry KJ: Evaluation of a brief cognitive-behavioral program for the prevention of chronic PTSD in recent assault victims. J Consult Clin Psychol 63:948-955, 1995

16. Foa EB, Meadows EA: Psychosocial treatments for posttraumatic stress disorder: A critical review. Annu Rev Psychol 48:449-480, 1997

17. DuHamel KN, Ostroff JS, Bovbjerg DH, et al: Trauma-focused intervention after bone marrow transplantation: A case study. Behav Therapy 31: 175-186, 2000

18. Weathers FW, Litz BT, Herman DS, et al: The PTSD checklist (PCL): Reliability, validity, and diagnostic utility. Presented at the International Society for Traumatic Stress Studies, San Antonio, TX, October 24-27, 1993

19. Derogatis LR: Brief Symptom Inventory: Administration, Scoring, and Procedures Manual (ed 3). Minneapolis, MN, National Computer Systems, 1993

20. Callahan CM, Unverzagt FW, Hui SL, et al: Six-item screener to identify cognitive impairment among potential subjects for clinical research. Med Care 40:771-781, 2002

21. First MB, Spitzer RL, Gibbon M, et al: Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition With Psychotic Screen (SCID-I/P W/PSY SCREEN). New York, NY, Biometrics Research, New York State Psychiatric Institute, 2002

22. Beck AT, Ward CH, Mendelson M, et al: An inventory for measuring depression. Arch Gen Psychiatry 4:561-571, 1961

23. Brown GK: A Review of Suicide Assessment Measures for Intervention Research With Adults and Older Adults. Bethesda, MD, National Institute of Mental Health, 2000

24. Cherpitel CJ: A brief screening instrument for problem drinking in the emergency room: The RAPS4—Rapid Alcohol Problems Screen. J Stud Alcohol 61:447-449, 2000

25. Brown RL, Leonard T, Saunders LA, et al: A two-item conjoint screen for alcohol and other drug problems. J Am Board Fam Pract 14:95-106, 2001

26. Beck AT, Rush AJ, Shaw BF, et al: Cognitive Therapy of Depression. New York, NY, Guilford Press, 1979

27. Foa EB, Dancu CV, Hembree EA, et al: A comparison of exposure therapy, stress inoculation training, and their combination for reducing posttraumatic stress disorder in female assault victims. J Consult Clin Psychol 67:194-200, 1999

28. Lewis JA, Manne SL, DuHamel KN, et al: Social support, intrusive thoughts, and quality of life in breast cancer survivors. J Behav Med 24:231-245, 2001

29. Manne SL, Pape SJ, Taylor KL, et al: Spouse support, coping, and mood among individuals with cancer. Ann Behav Med 21:111-121, 1999

30. Roberts KJ, Lepore SJ, Helgeson V: Social-cognitive correlates of adjustment to prostate cancer. Psychooncology 15:183-192, 2006

31. Walker LG, Walker MB, Ogston K, et al: Psychological, clinical and pathological effects of relaxation training and guided imagery during primary chemotherapy. Br J Cancer 80:262-268, 1999

32. Blake DD, Weathers FW, Nagy LM, et al: A clinician's rating scale for assessing current and lifetime PTSD: The CAPS 1. Behavior Therapist 13:187-188, 1990

33. Blake DD, Weathers FW, Nagy LM, et al: The development of a clinician-administered PTSD scale. J Trauma Stress 8:75-90, 1995

34. Manne SL, Andrykowski MA: Are psychological interventions effective and accepted by cancer patients? II. Using empirically supported therapy guidelines to decide. Ann Behav Med 32:98-103, 2006

35. Brothers BM, Andersen BL: Hopelessness as a predictor of depressive symptoms for breast cancer patients coping with recurrence. Psychooncology 18:267-275, 2009

36. Pistrang N, Barker C: The partner relationship in psychological response to breast cancer. Soc Sci Med 40:789-797, 1995

37. Prieto JM, Saez R, Carreras E, et al: Physical and psychosocial functioning of 117 survivors of bone marrow transplantation. Bone Marrow Transplant 17:1133-1142, 1996

38. Mosher CE, DuHamel KN, Rini CM, et al: Barriers to mental health service use among hematopoietic SCT survivors. Bone Marrow Transplant 45:570-579, 2010

39. Australian Centre for Posttraumatic Mental Health: Australian Guidelines for the Treatment of adults With Acute Stress Disorder and Posttraumatic Stress Disorder. Melbourne, Victoria, Australian Centre for Posttraumatic Mental Health, 2007