

ORIGINAL ARTICLE

Check your sleep before you start: A secondary analysis of a stress management intervention for caregivers of stem cell transplant patients

Scott G. Ravyts¹ | Timothy S. Sannes^{2,3}  | Joseph M. Dzierzewski¹ |
Eric S. Zhou^{2,3}  | Benjamin W. Brewer⁴ | Crystal Natvig⁵ | Mark L. Laudenslager⁵

¹Department of Psychology, Virginia Commonwealth University, Richmond, Virginia, USA

²Dana-Farber Cancer Institute, Boston, Massachusetts, USA

³Department of Psychosocial Oncology and Palliative Care, Harvard Medical School, Boston, Massachusetts, USA

⁴Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

⁵University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

Correspondence

Timothy S. Sannes, Department of Psychiatry, Dana-Farber Cancer Institute, 75 Francis St, Boston, MA 02115, USA.

Email: TimothyS_Sannes@DCFI.HARVARD.EDU

Funding information

Patient-Centered Outcomes Research Institute, Grant/Award Number: CE1304-6208; National Institute on Aging, Grant/Award Number: K23AG049955

Abstract

Objective: Caregiving for hematopoietic stem cell transplant (HSCT) patients is associated with significant physical and psychological sequelae. While psychosocial interventions may reduce caregiver burden, knowledge regarding which caregivers may benefit the most from such interventions is limited. The purpose of this secondary analysis was to examine whether HSCT caregivers' peritransplant sleep moderated the effect of a psychosocial intervention on depression and anxiety posttransplant.

Methods: Participants included 135 caregivers (mean age = 54.23) who participated in randomized controlled trial and were assigned to receive either 8 weeks of Psychoeducation, Paced Respiration, and Relaxation (PEPRR) or treatment as usual (TAU). Sleep, depression, and anxiety were assessed using the Pittsburgh Sleep Quality Index, the Center for Epidemiologic Studies Depression Scale, and the State-Trait Anxiety Inventory, respectively. Caregiver symptoms were assessed at baseline (e.g., peritransplant period) and 6-month posttransplant.

Results: Baseline sleep quality ($\Delta R^2 = 0.04$, $p = 0.002$), sleep efficiency ($\Delta R^2 = 0.03$, $p = 0.02$), and sleep onset latency ($\Delta R^2 = 0.07$, $p < 0.001$) independently moderated the effect of group assignment on depression outcomes at the 6-month follow-up. Specifically, caregivers with poor sleep at baseline who received PEPRR reported significantly lower depression scores at follow-up compared to caregivers with poor sleep who received TAU. By contrast, only sleep quality ($\Delta R^2 = 0.02$, $p = 0.01$) and sleep onset latency ($\Delta R^2 = 0.02$, $p = 0.005$) moderated the effect of the group assignment on anxiety.

Conclusions: Psychosocial interventions for HSCT caregivers may buffer against psychological morbidity, particularly among caregivers with poor sleep quality.

KEYWORDS

anxiety, cancer, caregivers, depression, hematopoietic stem cell transplantation, psychoncology, sleep

Hematopoietic stem cell transplantation (HSCT) is an intensive medical procedure designed to treat hematological malignancies, as well as nonmalignant diseases sensitive to immune modulation. The procedure consists of replacing damaged or destroyed cells with either autologous (self-donor) or allogeneic (alternative donor) stem cells. Both treatments are arduous, with allogeneic patients hospitalized for nearly a month while autologous patients require less than 2 weeks of hospitalization following the procedure.¹ While the treatment is associated with extended life expectancy overall, adverse side effects are common and include infection, organ-specific complications, graft versus host disease, and secondary cancers, resulting in decreased quality of life.²

1 | HSCT CAREGIVERS

Family caregivers are increasingly expected by healthcare programs to play a significant role in the recovery of HSCT patients.³ HSCT caregivers, in particular, are closely involved in this process since they are expected to provide emotional support, administer medications, monitor vital signs, and coordinate patients' medical appointments for many months following hospital discharge. This crucial support of the patient is frequently not without consequence as HSCT caregivers experience higher rates of depression, anxiety, and sleep disorders, as well as lower quality of life relative to the general population.^{4,5} In fact, depression and anxiety symptoms among HSCT caregivers are comparable to that of their patients.^{6,7} Yet, despite experiencing similar levels of adverse mental health consequences, HSCT caregivers are less likely than their care recipients to receive mental health treatment.⁶

2 | PSYCHOSOCIAL INTERVENTIONS FOR HSCT CAREGIVERS

A small, but growing, number of psychosocial interventions have focused on improving HSCT caregiver well-being. Treatments have commonly consisted of psychoeducation, coping skills training, and health behavior promotion, with the authors of a recent systematic review of psychosocial interventions for HSCT caregivers finding partial support for improvements in caregiver depression, anxiety, coping, and quality of life.⁸ Yet, the availability of these interventions remain limited.⁹ In light of these outcomes and the limited availability of such support programs, additional research is needed to identify which caregivers are the most likely to benefit from these psychosocial interventions.

3 | PREVALENCE AND CONSEQUENCES OF SLEEP DISTURBANCE AMONG HSCT CAREGIVERS

Given the prevalence and adverse mental health consequences associated with poor sleep among caregivers, further examination of

sleep in HSCT caregivers may be beneficial.^{10,11} Over two thirds of HSCT caregivers report poor sleep quality pretransplant.¹⁰ This is likely due to caregiving duties and major life disruption leading up to transplant. There is also some suggestion that caregivers' sleep relates to important clinical outcomes in the patients for whom they care,¹² as well as indications that alteration of sleep in HSCT caregivers can influence mood, affect, and physiologic functioning.¹³ Sleep concerns in HSCT caregivers are frequently left untreated with less than 3% receiving medication for sleep in one study.¹⁴ Moreover, consistent with the refractory nature of insomnia, sleep disturbance among HSCT caregivers appears to persist years after the transplant, with caregivers reporting a rate of sleep disorders more than four times that of the general population.⁵

Among the general population, sleep disturbance is a well-known prospective risk factor for both depression and anxiety.^{15,16} These associations extend to non-HSCT cancer caregivers as well.¹⁷ For example, researchers of one study found that sleep quality, sleep efficiency, and daytime dysfunction accounted for nearly two thirds of cancer caregivers' depression scores.¹⁸ Thus, caregivers with greater sleep disturbance may be at a higher risk for experiencing adverse mental health outcomes and may therefore be more likely to benefit from psychosocial interventions designed to mitigate caregiver stress.

4 | PRESENT STUDY

The aim of the present study was to examine whether HSCT caregivers with varying levels of sleep disturbance during the peritransplant period would differ in regards to the effect of a psychosocial intervention on depression and anxiety. In order to examine this aim, data from a randomized control trial in which HSCT caregivers received either a brief psychosocial intervention or treatment as usual (TAU) were analyzed.¹⁹ While researchers from the parent study found that caregivers receiving the psychosocial intervention reported reduced caregiver distress, knowledge regarding which caregivers benefited the most such treatment remains unknown. Given the high prevalence of sleep disturbance among HSCT caregivers and its association with adverse mental health outcomes, it was hypothesized that caregivers with greater sleep disturbance at baseline (i.e., during the peritransplant period) who received the psychosocial intervention would report greater improvements in depression and anxiety at 6-month posttransplant relative to caregivers with better sleep.

5 | METHODS

5.1 | Participants

Data for the present secondary data analysis were obtained as part of a larger randomized control trial examining the effect of a psychosocial intervention on HSCT caregiver burden and quality of life

of Allo-HSCT patients.¹⁹ The primary outcomes of the parent study were patients' quality of life and caregivers' distress. In total, 159 patients and their caregivers were recruited between March 2014 and November 2016 during pretransplant screening at either a community-transplant program or a university-based cancer center. Although a sample size of 224 dyads was sought based on a prior psychosocial intervention among this patient population,²⁰ the recruitment goal was not met within the time allotted by the funding agency.

Eligibility criteria for the parent study included both the patient and the caregiver agreeing to participate in the study, being 18 years or older, speaking and reading English, and having telephone access. In addition, caregivers needed to be willing to use a smartphone and participate in intervention sessions if randomized to the intervention group. To qualify as a caregiver, individuals had to identify as being the primary person responsible for the patient posttransplant, operationalized as being emotionally invested in the patient and responsible for major decisions involving the patient's care by self-report. Participants were screened and enrolled by site psycho-oncologists.

5.2 | Procedures

The design of the parent study is briefly summarized below and described in depth elsewhere.¹⁹ A permuted block design was used by the project statistician to randomize participants to either the treatment condition entitled Psychoeducation, Paced Respiration, and Relaxation (PEPRR) or TAU. Group assignments were placed in a sealed envelope by the project manager and assigned only after completion of baseline questionnaires (i.e., peritransplant) with additional follow-up assessments of participants' health and well-being completed 1.5-, 3-, and 6-month posttransplant. All study team members, aside from site supervisors and interventions, remained blinded to group assignment until the end of the study. The parent study was approved by the Colorado Multi-Institutional Review Board (IRB approval no. 13-2639) and registered at [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT02037568). All participants provided informed consent. A consort diagram for the parent study and this secondary analysis is presented in Figure 1.

Caregivers assigned to PEPRR received eight semi-structured one-on-one sessions with a master's level social worker. Sessions were available to caregivers during the first 100 days posttransplant with participants receiving the first session an average of 2 weeks posttransplant. The first four sessions occurred on a weekly basis while the remaining sessions occurred biweekly.

Each PEPRR session lasted 60–75 min and consisted of the following modules: (1) introduction to the program, instructions for using a biofeedback device, and overview of stress consequences, (2) psychoeducation about stress and the mind–body connection, (3) exploring the relationship between thoughts, emotions, and stress, (4) effective coping strategies for stress, (5) maintaining key health behaviors, (6) managing uncertainty and lack of control, (7) improving

communication and navigating changing roles, and (8) using social support effectively. Session 5 briefly reviewed sleep hygiene and the importance of physical activity. Participants assigned to TAU received sections of the workbook associated with PEPRR via email. These sections were provided on a weekly basis for the first month and then a biweekly basis during the last 2 months. TAU received weekly phone calls to ensure the workbook sections were received and as a contact control.

5.3 | Measures

Demographic characteristics. Participants self-reported demographic information including age, sex, race, ethnicity, and relationship to their care recipient. Information pertaining to the patients' medical condition was extracted from their medical charts.

Sleep. Self-reported sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI).²¹ The PSQI captures sleep quality in the past month across seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. This well-validated and commonly used measure of sleep consists of 19 items. Total scores range from 0 to 21, with scores equal to or greater than 5 indicative of poor sleep quality.²¹ The PSQI has been widely used among caregivers,²² and has a sensitivity and specificity of 89.6% and 86.5%, respectively.²¹ Cronbach's α for the PSQI at baseline was acceptable (0.71).

Depression. Depression was assessed via the Center for Epidemiologic Studies Depression Scale (CES-D).²³ This scale consists of 20 items and ranges from 0 to 60 with higher scores indicating greater depressive symptomology. Scores of 16 or higher are suggestive of clinical depression.²³ The CES-D has a diagnostic sensitivity of 87% and a specificity of 70%.²⁴ As previously reported,¹⁹ Cronbach's α was good (0.81) across assessments.

Anxiety. Anxiety was assessed using the State-Trait Anxiety Inventory (STAI).²⁵ The state version of the STAI used within this study (i.e., STAI-S), is comprised of 40 items which are rated on a 4-point Likert scale from 1 (*Not at all*) to 4 (*Very Much So*). Total scores range from 20 to 80 with higher scores representing greater anxiety. Cronbach's α was excellent (0.95) across assessments.

5.4 | Data analyses

Data analyses were conducted using SPSS v26 and hypothesized moderation models were conducted using PROCESS Macro v3.5.²⁶ Only caregivers who completed the PSQI at baseline were included in the present study. Missing data at follow-up were handled using expectation maximization (EM).²⁷ As one of the maximum likelihood approaches, EM uses observed data to calculate estimate parameters, which are then used to predict missing data.

Eight moderation analyses using generalized linear modeling with ordinary least squares regression were conducted using Model 1

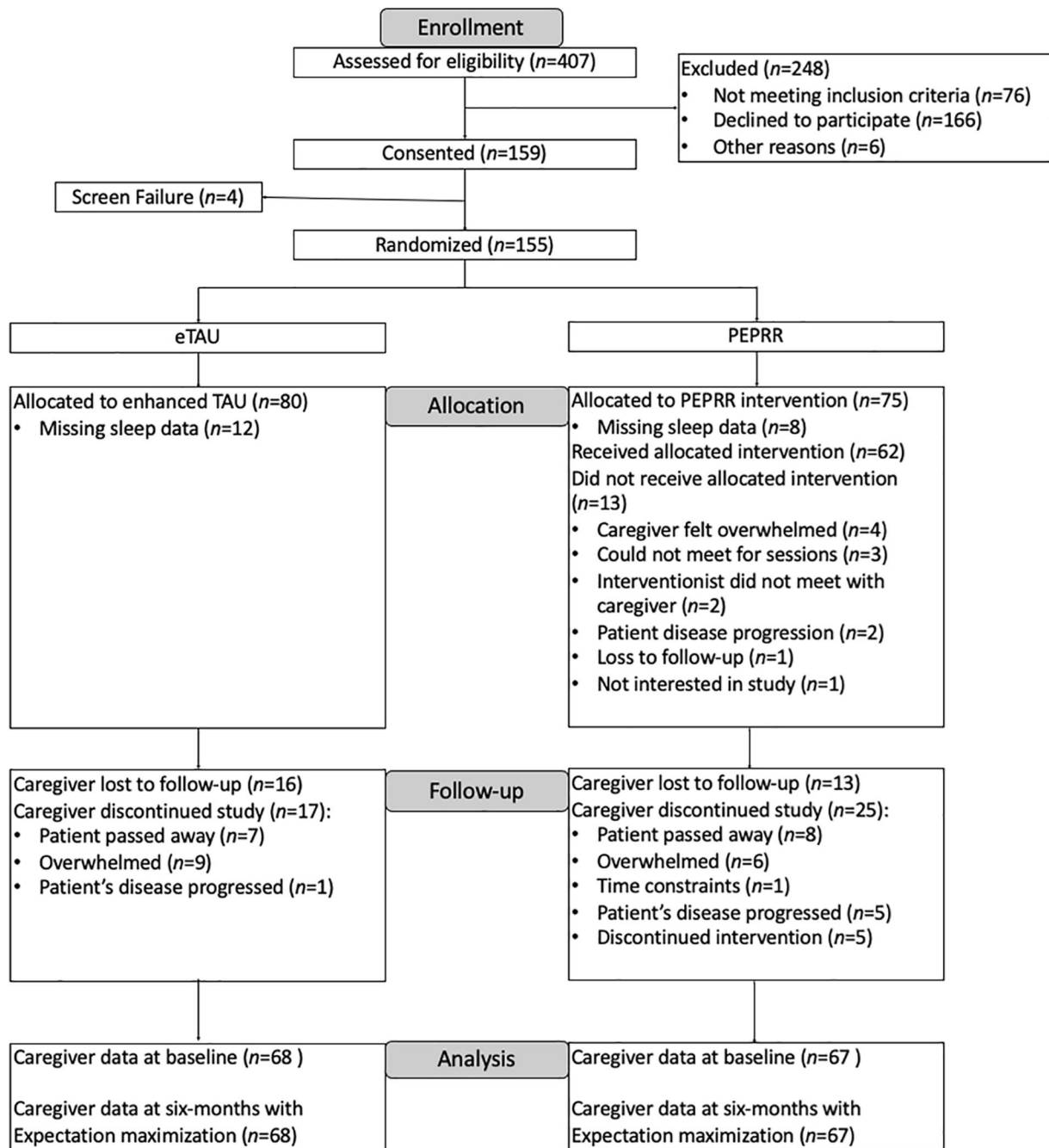


FIGURE 1 CONSORT diagram

in PROCESS Macro. For all models, treatment condition (i.e., PEPRR or TAU) was entered as the independent variable with age and baseline depression or anxiety scores included as covariates. Age was included as an a priori covariate due to its known relationships with both depression and sleep.^{20,28} Depression and anxiety, as measured by the CES-D and STAI-S 6-month posttransplant, were entered as the respective outcome variables for each of four models. This time point was chosen given the limited knowledge surrounding long-term mental health outcomes among HSCT caregivers. Moderation effect sizes were reported via the change in R^2 which represents the

increase in variance explained by the model with the inclusion of the product term (i.e., IV X moderator interaction) compared to the model without the product term.²⁶

Four sleep components from participants' peritransplant baseline assessment using the PSQI were selected as the moderator variables. These components included overall sleep quality (PSQI total score), self-reported sleep duration (expressed in hours), sleep efficiency (a commonly used clinical metric calculated by dividing total time spent sleeping over total time in bed), and sleep onset latency (expressed in minutes). Each sleep component was entered as the sole moderator

in two models, one assessing depression and another assessing anxiety. Significant moderation effects were further evaluated using the Johnson-Neyman (J-N) technique which determines the point at which a continuous moderator variable significantly affects the relationship between an independent variable and dependent variable.²⁶

6 | RESULTS

6.1 | Participant characteristics

The final analytic sample consisted of 135 caregivers. This total sample size was slightly reduced compared to the parent study that did not originally target sleep as a secondary outcome.¹⁹ The PSQI as a secondary outcome was added a few months after study recruitment began and thus some participants did not provide a peritransplant assessment (baseline). Participants were predominately White (90.77%) middle-aged (mean [M] = 52.23, standard deviation [SD] = 13.74) females (77.03%). Mean scores on the modified CES-D at baseline were above the clinical cut-off of 16 (M = 20.28, SD = 6.70), suggestive of risk for clinically significant depressive symptoms. Similarly, participants' average score on the PSQI was above the recommend cut-off score of 5 (M = 7.88, SD = 3.92), indicative of poor overall sleep quality. Little's MCAR test was nonsignificant, $\chi^2 = 40.42$, $df = 53$, $p = 0.90$, indicating that missing data at follow-up were suitable for EM. Complete participant characteristics are presented in Table 1.

6.2 | Sleep quality and mental health symptoms

Caregiver baseline sleep quality significantly moderated the relationship between group assignment and depression at the 6-month follow-up ($\Delta R^2 = 0.04$, $b = -0.63$, $SE = .20$, $p = 0.002$). Based on J-N results, group assignment significantly affected depression for participants with PSQI scores above 7.66 (51.85% of the total sample). Baseline sleep quality also moderated the effect of anxiety at follow-up ($\Delta R^2 = 0.02$, $b = -0.88$, $SE = 0.32$, $p = 0.01$), with J-N results indicating that group assignment significantly affected anxiety for participants with PSQI scores above 8.38 (45.92% of the total sample).

6.3 | Sleep duration and mental health symptoms

In contrast to sleep quality, sleep duration at baseline failed to moderate the relationship between group assignment and depression at 6-month follow-up ($\Delta R^2 = 0.01$, $b = 0.80$, $SE = 0.46$, $p = 0.21$). Similarly, sleep duration did not moderate the relationship between group assignment and anxiety ($\Delta R^2 < .01$, $b = 0.18$, $SE = 1.01$, $p = 0.86$).

6.4 | Sleep efficiency and mental health symptoms

Sleep efficiency at baseline moderated the relationship between group assignment and depression at the 6-month follow-up ($\Delta R^2 = 0.03$, $b = 0.16$, $SE = 0.07$, $p = 0.02$). Specifically, according to J-N results, the effect of group assignment on depression was significant for participants with a sleep efficiency below 84.06 (47.37% of the total sample). By contrast, sleep efficiency failed to moderate the effect of group assignment on anxiety ($\Delta R^2 = 0.01$, $b = 0.13$, $SE = 0.11$, $p = 0.22$).

6.5 | Sleep onset latency and mental symptoms

Finally, sleep onset latency at baseline also moderated the relationship between group assignment and depression at 6-month follow-up ($\Delta R^2 = 0.07$, $b = -0.13$, $SE = 0.02$, $p < 0.001$). Based on J-N results, the effect of group assignment on caregiver depression was significant for participants with a sleep onset latency greater than 23.15 min (38.35% of the total sample). Sleep onset latency also moderated the relationship between group assignment and anxiety at follow-up ($\Delta R^2 = 0.02$, $b = -0.16$, $SE = 0.06$, $p = 0.005$). The effect of group assignment on anxiety was significant for participants with a sleep onset latency above 26.27 min (38.34% of the total sample). Please see Figure 2 for a graphical depiction of the moderating effects of baseline sleep on depression and anxiety at follow-up. The complete moderating effects are presented in Table 2.

7 | DISCUSSION

The purpose of the present study was to examine whether HSCT caregivers' peritransplant sleep moderated the effect of a psychosocial intervention on caregiver depression and anxiety at follow-up. Consistent with our hypotheses, caregivers' sleep quality, sleep efficiency, and sleep onset latency at baseline each independently moderated the effect of the psychosocial intervention on caregivers' depressive symptoms 6 months later. Specifically, caregivers with poor sleep at baseline who received the psychosocial intervention reported significantly lower depressive symptoms posttransplant compared to caregivers with poor sleep at baseline who received TAU. Receiving PEPRR appeared to buffer the impact of sleep disturbance at baseline on depressive's symptoms at follow-up. Contrary to our hypotheses, sleep duration did not moderate the effect of the intervention on depressive symptoms. Finally, only sleep quality and sleep onset latency moderated the effect of the intervention on caregivers' anxiety.

The present findings align with existing literature in which researchers found that sleep disturbance often acts as a prodromal symptom of depression.²⁹ This phenomenon may be the result of the shared biological underpinnings of both sleep disturbance and depression.³⁰ Behaviorally, Spielman's 3P model of insomnia describes how predisposing, precipitating, and perpetuating factors

TABLE 1 Participant descriptive characteristics at baseline

	Total (n = 135)	TAU (n = 68)	PEPRR (n = 67)
Age	54.23 (13.74)	54.70 (12.37)	53.75 (15.08)
Sex, number (%)			
Female	104 (77.03)	54 (79.41)	50 (74.63)
Male	31 (22.96)	14 (20.59)	17 (25.37)
Ethnicity			
Hispanic/Latino	12 (9.37)	7 (10.77)	5 (7.93)
Non-Hispanic/Latino	116 (90.62)	58 (89.23)	58 (92.06)
Race			
White	118 (90.77)	62 (91.12)	56 (90.32)
Black	2 (1.54)	0 (0.00)	2 (3.22)
Other	10 (7.69)	6 (8.82)	4 (6.45)
Relationship to care recipient, number (%)			
Spouse/civil partner	90 (66.66)	49 (72.05)	41 (61.12)
Parent	19 (14.07)	10 (14.70)	9 (13.43)
Sibling	10 (7.41)	3 (4.41)	7 (10.45)
Other	16 (11.86)	6 (8.82)	10 (14.92)
Care recipient diagnosis, number (%)			
Leukemia	81 (60.00)	41 (60.29)	40 (59.70)
Lymphoma	18 (13.33)	11 (16.18)	7 (10.45)
MDS/MPS	31 (22.96)	14 (20.59)	17 (25.37)
Other	5 (3.70)	2 (2.94)	3 (4.48)
Mental health symptoms			
CES-D total score	20.28 (6.70)	19.88 (6.87)	20.69 (6.56)
STAI-S total score	40.59 (12.96)	39.22 (11.49)	42.00 (14.27)
Sleep			
PSQI total score	7.99 (3.92)	8.20 (4.18)	7.78 (3.67)
Sleep duration	6.66 (1.29)	6.62 (1.30)	6.71 (1.30)
Sleep efficiency	82.56 (12.28)	82.33 (12.98)	82.79 (11.64)
Sleep onset latency	25.64 (22.07)	26.20 (23.66)	25.09 (20.55)

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; PEPRR, Psychoeducation, Paced Respiration, and Relaxation; PSQI, Pittsburgh Sleep Quality Index; STAI, State-Trait Anxiety Inventory; TAU, treatment as usual.

converge to bring about and maintain sleep disturbance.³¹ This model may provide a framework for understanding the moderating effect of sleep on depression outcomes. Although precipitating factors, such as the psychological distress stemming from caregiving leading into HSCT, may initially contribute to the onset of sleep disturbance, sleep disturbance is believed to be maintained by perpetuating factors (e.g., inconsistent schedules, daytime napping, spending excessive time in bed). The present intervention touched on practicing sleep hygiene and the importance of monitoring sleep, which may have driven some of the observed intervention or moderation effects. Receiving psychosocial support,

as in the intervention presented herein, shortly following transplant may limit the incidence of perpetuating factors which contribute to sleep disturbance and its depression-related consequences. Future studies may benefit from measuring both outcomes over time.

Our finding that sleep duration did not moderate the treatment effect of depression, thus, the quality rather than the duration of sleep may be a more important prodromal indicator of depression. This coincides with a previous study in which researchers found that, relative to sleep quality, sleep duration may be a less robust predictor of depression onset.³² One possible explanation for this findings may

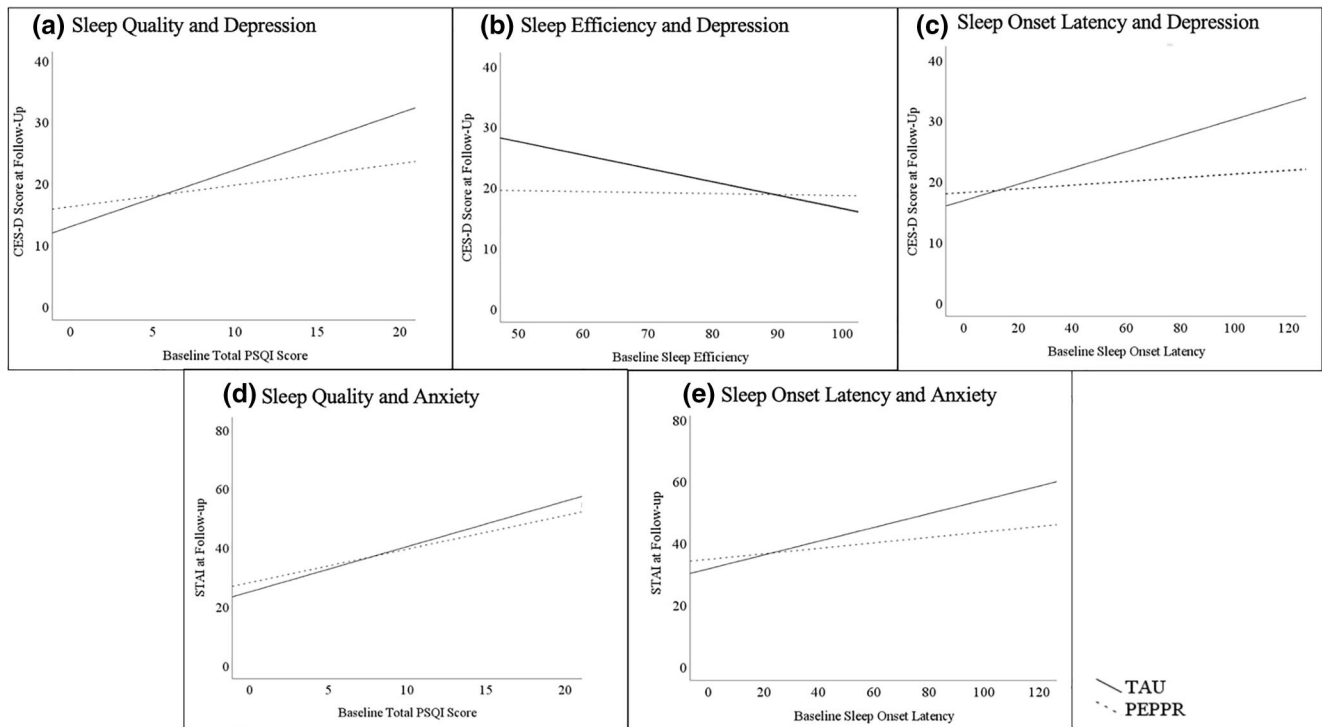


FIGURE 2 Caregiver depression as a function of baseline PSQI scores (A), sleep efficiency (B), and sleep onset latency (C). Caregiver anxiety as a function of baseline PSQI score (D) and sleep onset latency (E). Lower PSQI total scores indicate better sleep quality. PEPPR, Psychoeducation, Paced Respiration, and Relaxation; PSQI, Pittsburgh Sleep Quality Index; TAU, treatment as usual

be that depressed individuals often experience short (e.g., ≤ 6 h per night) or long sleep durations (e.g., ≥ 9 h per night).

Several reasons might explain why only some aspects of caregiver's peritransplant sleep moderated the effect of the intervention on anxiety outcomes. First, in contrast with a prior iteration of PEPPR which had the strongest effect size ($ES = 0.66$) for anxiety outcomes,²⁰ the effect size for anxiety in the parent study was smaller ($ES = 0.44$), thus making it harder to detect a moderating effect of sleep if one was present. This issue may have been further exacerbated by the fact that caregivers' average level of anxiety at baseline was only marginally above what is typically considered clinically significant (score above 40),³³ with 54.81% of the sample scoring below the standard cut-off. By contrast, 78.50% of the sample scored above the clinical cutoff for depression at baseline. In addition, much of the caregiving experience in preparing for HSCT involves significant anticipation and anxiety—often future-oriented mental states³⁴—which may subside naturally over the course of patients' transplant.³⁵ Depression, conversely, may be more amenable to intervention, potentially explaining the lack of an interaction for anxiety and group assignment.

7.1 | Clinical implications

Based on the results of the present study, additional screening of HSCT caregivers' sleep may be warranted. Sleep disturbance is known to be refractory, as evidenced by the high rates of sleep

disorders reported by HSCT caregivers years after transplant.⁵ Thus, despite inherent challenges in screening for caregiver distress while also focusing on the patient's well-being, early screening of sleep disturbance among HSCT caregivers could be clinically useful in identifying those most likely to benefit from psychosocial treatment.

If insomnia is the presenting disorder, HSCT caregivers may also benefit from behavioral sleep interventions. Cognitive behavior for insomnia (CBT-I) is considered the first-line of treatment for insomnia and is associated with improvements in sleep and depression among both caregivers and noncaregivers,^{36,37} yet only one CBT-I study was designed specifically for cancer caregivers.³⁶ While access to mental health treatment for HSCT caregivers may be limited, behavioral treatments for insomnia have been shown to be effective when delivered by nonspecialists.³⁸

7.2 | Study limitations

Several limitations of the present study are noteworthy. First, the study consisted of a predominately White sample. Racial and ethnic differences in the amount of time spent providing care, as well as in the mental health consequences associated care have been noted.³⁹ Thus, future research should address whether the current findings generalize to HSCT caregivers from racial and ethnic minority backgrounds. Second, caregiver sleep was limited to a single self-report measure of sleep quality making it susceptible to recall bias. Furthermore, the presence of other sleep disorders, such as sleep apnea, that contribute

TABLE 2 Moderation results for baseline sleep on 6-month depressive and anxiety outcomes

Depression				Anxiety			
	<i>b</i>	<i>SE</i>	<i>p</i> Value		<i>b</i>	<i>SE</i>	<i>p</i> Value
Age	0.01	0.03	0.77	Age	−0.03	0.05	0.44
Group assignment	3.24	1.79	0.07	Group assignment	4.88	2.8	0.08
Baseline sleep quality	0.67	0.14	<0.001	Baseline sleep quality	0.97	0.21	<0.001
Baseline CES-D	0.39	0.07	<0.001	Baseline STAI	0.59	0.05	<0.001
Group X sleep quality	−0.63	0.20	0.002	Group X sleep quality	−0.88	0.32	0.01
Total $R^2 = 0.42$				Total $R^2 = 0.61$			
	<i>b</i>	<i>SE</i>	<i>p</i> Value		<i>b</i>	<i>SE</i>	<i>p</i> Value
Age	0.01	0.03	0.80	Age	−0.03	0.05	0.48
Group assignment	−7.12	4.31	0.10	Group assignment	−3.58	6.84	0.60
Baseline sleep duration	−1.19	0.46	0.01	Baseline sleep duration	−1.15	0.72	0.11
Baseline CES-D	0.42	0.07	<0.001	Baseline STAI	0.62	0.05	<0.001
Group X sleep duration	0.80	0.46	0.21	Group X sleep duration	0.18	1.01	0.86
Total $R^2 = 0.34$				Total $R^2 = 0.57$			
	<i>b</i>	<i>SE</i>	<i>p</i> Value		<i>b</i>	<i>SE</i>	<i>p</i> Value
Age	0.002	0.03	0.94	Age	−0.04	0.05	0.45
Group assignment	−15.09	5.55	0.01	Group assignment	−13.22	8.92	0.14
Baseline sleep efficiency	−0.15	0.05	0.001	Baseline sleep efficiency	−0.14	0.07	0.06
Baseline CES-D	0.41	0.67	<0.001	Baseline STAI	0.62	0.05	<0.001
Group X sleep efficiency	0.16	0.07	0.02	Group X sleep efficiency	0.13	0.11	0.22
Total $R^2 = 0.35$				Total $R^2 = 0.57$			
	<i>b</i>	<i>SE</i>	<i>p</i> Value		<i>b</i>	<i>SE</i>	<i>p</i> Value
Age	0.003	0.03	0.93	Age	−0.04	0.05	0.37
Group assignment	1.56	1.19	0.19	Group assignment	1.82	1.92	0.35
Baseline sleep onset latency	0.12	0.02	<0.001	Baseline sleep onset latency	0.15	0.04	<0.001
Baseline CES-D	0.44	0.06	<0.001	Baseline STAI	0.62	0.05	<0.001
Group X sleep onset latency	−0.13	0.02	<0.001	Group X sleep onset latency	−0.16	0.06	0.005
Total $R^2 = 0.41$				Total $R^2 = 0.61$			

Abbreviations: *b*, beta weight coefficient; CES-D, Center for Epidemiologic Studies of Depression Scale; STAI, State-Trait Anxiety Inventory; *SE*, standard error.

to poorer quality sleep was not assessed. Researchers may also benefit from including objective or microlongitudinal measures of sleep in order to have a more nuanced understanding of the associations between sleep and mental health in this unique caregiving population. Finally, the relatively small sample size might have limited our ability to detect a moderating effect if one was present.⁴⁰

8 | CONCLUSION

Overall, the present study contributes to the extant literature by suggesting that psychosocial interventions for HSCT caregivers may

buffer the role of poor sleep in depression, and to a lesser extent anxiety, following transplant. Early identification of sleep disturbance among HSCT caregivers appears warranted given its association with depression in the months following transplant. Future HSCT caregiver interventions may also benefit from addressing whether targeting caregivers' insomnia symptoms confers additional mental health benefits.

ACKNOWLEDGMENTS

Research reported in this research was funded through a Patient-Centered Outcomes Research Institute (PCORI) contract (CE1304-6208) (Laudenslager) and supported in part by the National Institute

on Aging of the National Institutes of Health under Award Number K23AG049955 (Dzierzewski). The statements and opinions in this publication are solely the responsibility of the authors and do not necessarily represent the views of NIH or PCORI and its Board of Governors or Methodology Committee. The authors would like to honor the memory of Dr. Mark Laudenslager who dedicated much of his scientific career to identifying how caring for others can take a toll on one's own health.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

ORCID

Timothy S. Sannes  <https://orcid.org/0000-0003-4479-0350>

Eric S. Zhou  <https://orcid.org/0000-0003-1038-8961>

REFERENCES

- Broder MS, Quock TP, Chang E, et al. The cost of hematopoietic stem-cell transplantation in the United States. *Am Health Drug Benefits*. 2017;10(7):366-374.
- Majhail NS. Long-term complications after hematopoietic cell transplantation. *Hematol Oncol Stem Cell Ther*. 2017;10(4):220-227. <https://doi.org/10.1016/j.hemonc.2017.05.009>
- Applebaum AJ, Bevans M, Son T, et al. A scoping review of caregiver burden during allogeneic HSCT: lessons learned and future directions. *Bone Marrow Transplant*. 2016;51(11):1416-1422. <https://doi.org/10.1038/bmt.2016.164>
- Bevans MF, Ross A, Wehrlen L, et al. Documenting stress in caregivers of transplantation patients: initial evidence of HPA dysregulation. *Stress*. 2016;19(2):175-184. <https://doi.org/10.3109/10253890.2016.1146670>
- Jamani K, Onstad LE, Bar M, et al. Quality of life of caregivers of hematopoietic cell transplant recipients. *Biol Blood Marrow Transplant*. 2018;24(11):2271-2276. <https://doi.org/10.1016/j.bbmt.2018.06.015>
- Bishop MM, Beaumont JL, Hahn EA, et al. Late effects of cancer and hematopoietic stem-cell transplantation on spouses or partners compared with survivors and survivor-matched controls. *J Clin Oncol*. 2007;25(11):1403-1411. <https://doi.org/10.1200/JCO.2006.07.5705>
- Park S, Choi E-K, Kim I-R, Cho J, Jang JH. Comparison of quality of life and depression between hematopoietic stem cell transplantation survivors and their spouse caregivers. *Blood Res*. 2019;54(2):137-143. <https://doi.org/10.5045/br.2019.54.2.137>
- Bangerter LR, Griffin JM, Langer S, et al. The effect of psychosocial interventions on outcomes for caregivers of hematopoietic cell transplant patients. *Curr Hematol Malign Rep*. 2018;13(3):155-163. <https://doi.org/10.1007/s11899-018-0445-y>
- Frey P, Stinson T, Siston A, et al. Lack of caregivers limits use of outpatient hematopoietic stem cell transplant program. *Bone Marrow Transplant*. 2002;30(11):741-748.
- Sannes TS, Simoneau TL, Mikulich-Gilbertson SK, et al. Distress and quality of life in patient and caregiver dyads facing stem cell transplant: identifying overlap and unique contributions. *Support Care Cancer*. 2019;27(6):2329-2337. <https://doi.org/10.1007/s00520-018-4496-3>
- Ravyts SG, Dzierzewski JM. Sleep disturbance, mental health symptoms, and quality of life: a structural equation model assessing aspects of caregiver burden. *Clin Gerontol*. 2020. 1-10. <https://doi.org/10.1080/07317115.2020.1783042>
- Sannes TS, Mikulich-Gilbertson SK, Natvig CL, Brewer BW, Simoneau TL, Laudenslager ML. Caregiver sleep and patient neutrophil engraftment in allogeneic hematopoietic stem cell transplant. *Cancer Nurs*. 2018;41(1):77-85. <https://doi.org/10.1097/NCC.0000000000000447>
- Simoneau TL, Mikulich-Gilbertson SK, Natvig C, et al. Elevated peri-transplant distress in caregivers of allogeneic blood or marrow transplant patients. *Psychooncology*. 2013;22(9):2064-2070. <https://doi.org/10.1002/pon.3259>
- Ross A, Yang L, Klagholz SD, Wehrlen L, Bevans MF. The relationship of health behaviors with sleep and fatigue in transplant caregivers. *Psychooncology*. 2016;25(5):506-512. <https://doi.org/10.1002/pon.3860>
- Franzen PL, Buysse DJ. Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. *Dialogues Clin Neurosci*. 2008;10(4):473-481.
- Jansson-Fröjmark M, Lindblom K. A bidirectional relationship between anxiety and depression, and insomnia? A prospective study in the general population. *J Psychosom Res*. 2008;64(4):443-449. <https://doi.org/10.1016/j.jpsychores.2007.10.016>
- Geng H-M, Chuang D-M, Yang F, et al. Prevalence and determinants of depression in caregivers of cancer patients. *Medicine*. 2018; 97(39):e11863. <https://doi.org/10.1097/MD.00000000000011863>
- Carter PA, Chang BL. Sleep and depression in cancer caregivers. *Cancer Nurs*. 2000;23(6):410-415.
- Laudenslager ML, Simoneau TL, Mikulich-Gilbertson SK, et al. A randomized control trial of stress management for caregivers of stem cell transplant patients: effect on patient quality of life and caregiver distress. *Psychooncology*. 2019;28(8):1614-1623.
- Laudenslager ML, Simoneau TL, Kilbourn K, et al. A randomized control trial of a psychosocial intervention for caregivers of allogeneic hematopoietic stem cell transplant patients: effects on distress. *Bone Marrow Transplant*. 2015;50(8):1110-1118. <https://doi.org/10.1038/bmt.2015.104>
- Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatr Res*. 1989;28(2):193-213.
- Maltby KF, Sanderson CR, Lobb EA, Phillips JL. Sleep disturbances in caregivers of patients with advanced cancer: a systematic review. *Palliat Support Care*. 2017;15(1):125-140. <https://doi.org/10.1017/S1478951516001024>
- Radloff LS. The CES-D scale. *Appl Psychol Meas*. 1977;1(3):385-401.
- Vilagut G, Forero CG, Barbaglia G, Alonso J. Screening for depression in the general population with the Center for Epidemiologic Studies Depression (CES-D): a systematic review with meta-analysis. *PLoS One*. 2016;11(5):e0155431. <https://doi.org/10.1371/journal.pone.0155431>
- Spielberger CD. *Manual for the State-Trait Anxiety Inventory (STAI)*; 1983. <https://ubir.buffalo.edu/xmlui/handle/10477/1873>. Accessed October 3, 2016.
- Hayes AF. *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach*. Guilford Publications; 2017.
- Dempster AP, Laird NM, Rubin DB. Maximum likelihood from incomplete data via the EM Algorithm. *J R Stat Soc Ser B Methodol*. 1977;39(1):1-22.
- Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*. 2015;1(1):40-43. <https://doi.org/10.1016/j.sleh.2014.12.010>

29. Baglioni C, Battagliese G, Feige B, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. *J Affect Disord*. 2011;135(1):10-19. <https://doi.org/10.1016/j.jad.2011.01.011>
30. Fang H, Tu S, Sheng J, Shao A. Depression in sleep disturbance: a review on a bidirectional relationship, mechanisms and treatment. *J Cell Mol Med*. 2019;23(4):2324-2332. <https://doi.org/10.1111/jcmm.14170>
31. Spielman AJ, Caruso LS, Glovinsky PB. A behavioral perspective on insomnia treatment. *Psychiatric Clin North Am*. 1987;10(4):541-553.
32. Bao Y-P, Han Y, Ma J, et al. Cooccurrence and bidirectional prediction of sleep disturbances and depression in older adults: meta-analysis and systematic review. *Neurosci Biobehav Rev*. 2017;75:257-273. <https://doi.org/10.1016/j.neubiorev.2017.01.032>
33. Knight RG, Waal-Manning HJ, Spears GF. Some norms and reliability data for the State-Trait Anxiety Inventory and the Zung Self-Rating Depression scale. *Br J Clin Psychol*. 1983;22(Pt 4):245-249. <https://doi.org/10.1111/j.2044-8260.1983.tb00610.x>
34. Rinaldi L, Locati F, Parolin L, Girelli L. *Distancing the Present Self from the Past and the Future: Psychological Distance in Anxiety and Depression*. London, UK: SAGE Publications; 2017.
35. Fife BL, Huster GA, Cornetta KG, Kennedy VN, Akard LP, Broun ER. Longitudinal study of adaptation to the stress of bone marrow transplantation. *J Clin Oncol*. 2000;18(7):1539-1549. <https://doi.org/10.1200/JCO.2000.18.7.1539>
36. Carter PA. A brief behavioral sleep intervention for family caregivers of persons with cancer. *Cancer Nurs*. 2006;29(2):95-103.
37. Manber R, Bernert RA, Suh S, Nowakowski S, Siebern AT, Ong JC. CBT for insomnia in patients with high and low depressive symptom severity: adherence and clinical outcomes. *Focus*. 2014;12(1):90-98. <https://doi.org/10.1176/appi.focus.12.1.90>
38. Alessi C, Martin JL, Fiorentino L, et al. Cognitive behavioral therapy for insomnia in older veterans using nonclinician sleep coaches: randomized controlled trial. *J Am Geriatr Soc*. 2016;64(9):1830-1838. <https://doi.org/10.1111/jgs.14304>
39. Fabius CD, Wolff JL, Kasper JD. Race differences in characteristics and experiences of Black and White caregivers of older Americans. *Gerontologist*. 2020;60:1244. <https://doi.org/10.1093/geront/gnaa042>
40. Aiken LS, West SG, Reno RR. *Multiple Regression: Testing and Interpreting Interactions*. SAGE; 1991.

How to cite this article: Ravvits SG, Sannes TS, Dzierzewski JM, et al. Check your sleep before you start: A secondary analysis of a stress management intervention for caregivers of stem cell transplant patients. *Psycho-Oncology*. 2021;30:936–945. <https://doi.org/10.1002/pon.5680>