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Caregiver Sleep and Patient Neutrophil Engraftment in Allogeneic Hematopoietic Stem Cell Transplant: A Secondary Analysis

Timothy S. Sannes, PhD, Susan K. Mikulich-Gilbertson, PhD, Crystal L. Natvig, BA, Dr. Benjamin W. Brewer, PsyD, Teresa L. Simoneau, PhD, and Mark L. Laudenslager, PhD

Departments of Psychiatry (Sannes, Mikulich-Gilbertson, Natvig and Laudenslager), General Internal Medicine (Sannes), and Department of Medicine (Dr. Brewer) University of Colorado Denver, Anschutz Medical Campus Aurora, CO; VA Eastern Colorado Health Care System, Denver CO (Simoneau)

Abstract

Background—Caregiving for allogeneic hematopoietic stem cell transplant (Allo-HSCT) patients can be significantly burdensome. Caregiver well-being often mirror patients' suffering. However, to our knowledge, this dyadic relationship has not been linked to patient outcome.

Objective—Caregiver's objective and subjective sleep and overall distress prior to transplantation were hypothesized to be related to patient's time to engraftment in secondary analyses.

Methods—Dyads ($N=124$) were Allo-HSCT patients (M age = 49.2; $SD = 12.7$) and their caregivers (M age=52.7; $SD = 12.3$). Caregiver's subjective sleep quality was measured via the Pittsburgh Sleep Quality Index, objective sleep was measured by actigraphy, and distress was measured by combining validated psychological measures.

Results—Both caregiver reports of worse sleep ($\beta = .22$; $p < .05$) and objective measurement of caregiver sleep patterns (higher sleep efficiency; less time awake after sleep onset) collected before engraftment significantly predicted shorter time to patient engraftment (β 's = $-.34$ and $.29$, respectively; p 's $< .05$). Caregiver distress was unrelated to engraftment ($\beta = .14$; $p = .22$).

Conclusions—Despite limitations in available patient data, these findings appear to link caregiver well-being to patient outcome. This underscores the interrelatedness of the patient-caregiver dyad in Allo-HSCT. Future research should examine psychological and biomedical mediators.

Corresponding Author: Timothy S. Sannes, PhD, Department of Psychiatry, University of Colorado Denver, Anschutz Medical Campus, RC-2, Room 3410A; Mailstop: C268-09, 12700 E. 19th Ave Aurora, CO 80045 (timothy.sannes@ucdenver.edu).

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All statements in this report, including its findings and conclusions, are solely those of the authors and do not necessarily represent the views of the Patient-Centered Outcomes Research Institute (PCORI), its Board of Governors or Methodology Committee as well as the NIH.

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Implications for Practice—Given that caregiver well-being during the peri-transplant period was associated with patient outcome in this study, such findings highlight the need to address caregiver and patient well-being during Allo-HSCT. There may be potential to improve patient outcome by focusing on the caregiver, which nursing staff is well-positioned to monitor.

Keywords

Caregiving; stress; time to engraftment; sleep; aging

Background

The psychological experience of cancer can be stressful for patients and their informal (e.g., unpaid) caregivers alike¹. Although both members of patient-partner dyads demonstrate elevated depressive symptoms and sleep problems compared to controls², cancer caregivers' psychological disturbance often directly mirrors the patients' psychological well-being and distress¹. Given this significant overlap, some have suggested that assessing caregiver symptom distress may be an adequate representation of patient distress when patient ratings are unavailable³. This observation is particularly important for nurses, who interact with these dyads regularly throughout the patients' care. Moreover, psychological problems in advanced cancer patients confers a 7.9 fold risk for meeting diagnostic criteria for a psychiatric disorder in the caregiver⁴. This further highlights the emotional connection between patients and caregivers. Dyads facing hematopoietic stem cell transplant (HSCT) represent an important clinical population for studying how similar relationships within dyads may be related to clinical outcomes in the patient.

Stem cell transplants for hematologic malignancies represent a clinical population in which the patient-caregiver dyad relationship is particularly important. Specifically, allogeneic HSCT (Allo-HSCT), while offering a potential cure from hematologic malignancy, is characterized by an intensive, lengthy and difficult treatment process that holds risk of significant side effects and death⁵. A number of important endpoints are related to successful recovery one of which is neutrophil engraftment (absolute neutrophil count greater than 500) occurring, on average, 18 days after myeloablation of the bone marrow⁶. Given the intensity of the transplant procedure, Allo-HSCT requires identification of an informal, caregiver – in addition to paid medical staff including nurses. The informal caregiver juggles a multitude of responsibilities (monitoring patient for infection and fevers, tracking complex medication regimens, provision of specialized dietary restrictions, and providing transportation) for more than 100 days⁷. Associated with these added duties, caregivers of Allo-HSCT patients report significant anxiety and elevated depressive symptoms compared to published norms⁸, and often meet criteria for other mental health problems⁹. Following transplant, partners reported less social support, dyadic satisfaction and spiritual well-being than their patients 6.7 years later². Similar results found higher levels of depression and anxiety in caregivers than their respective patients during the year following transplant¹⁰. Despite these data underscoring the interrelatedness of patient-caregiver dyads in Allo-HSCT, very few investigators have extended this relationship to exploring patient outcome in dyads facing Allo-HSCT. A mixed sample of autologous and allogeneic stem cell transplant showed that partner-related coping had the greatest positive impact on patient adjustment over the course

of treatment¹¹. The question remains of whether clinically meaningful outcomes for the patients, such as time to engraftment in Allo-HSCT, could be predicted by caregiver variables. Such data could inform interventions for caregivers, underscore the importance of nurses' ability to monitor well-being within dyads, and, potentially, improve patient outcome.

Conceptual Model

A number of recent models^{12,13} outline how HSCT patients, and the peri-transplant period, represent a unique timeframe to study psychosocial factors and relationships to clinical outcomes. In brief, this period represents a time in which psychosocial factors may be strongly related to clinical outcomes, given the importance of timely immune reconstitution coupled with the high distress experienced by patients¹⁰. In support of this model, results have emerged linking pre-transplant patient distress to time to engraftment in autologous HSCT¹⁴. Similar results in a sample of both Auto and Allo-HSCT patients¹³ demonstrated that greater optimism and less anxiety were associated with reduced time to neutrophil engraftment. Considering the overlapping characteristics within patient-caregiver dyads suggested by the models described above, caregiver well-being may be related to *patient* outcome. This conceptual framework in Figure 1 in which patient and caregiver well-being both contribute to patients' medical outcome such as neutrophil engraftment. Nursing staff form one of the front lines of surveillance by monitoring the well-being of patients and their caregivers, therefore this model suggests symptoms to track, monitor or therapeutically target which may impact patient medical outcomes. To our knowledge, no studies have applied indicators of caregiver well-being (such as sleep) as a proxy for examining patient clinical course (time to engraftment) in Allo-HSCT patients. The current study targets Allo-HSCT patients and assessment of their caregivers' well-being as an initial step towards supporting this model.

It has been previously reported⁸ elevated distress, poor sleep, anxiety, depression and avoidance behaviors in Allo-HSCT caregivers. While this group of caregivers demonstrated significant psychological benefit following an 8-session cognitive behavioral stress management intervention compared to treatment as usual¹⁵, an additional question is whether caregiver well-being assessed *prior* to randomization was related to patient outcome after transplant. The selection of predictor and outcome variables was guided by available data represented in our conceptual model (Figure 1) and the empirical literature. Specifically, sleep disturbance has been noted as the most common symptom of disrupted well-being among caregivers for early stage cancer patients¹⁶ with prevalence rates of clinically significant sleep disruption reaching as high as 95 percent¹⁷. Thus across domains of caregiver well-being that are often correlated in caregivers such as depression being correlated with sleep and vice versa¹⁸, sleep is particularly relevant to caregiver well-being¹⁶. Objective and subjective measures of caregiver sleep disturbance collected as part of the study were selected as predictor variables. We were also interested in the potential contribution of caregiver well-being more generally. Therefore, to reduce the number of statistical comparisons, a previously calculated caregiver distress composite score¹⁵ that combined validated several psychological measures of stress, depression, and anxiety by principle components analysis was selected as an additional predictor variable of distress.

Due to limitations in available data regarding the patients in this study and its importance in predicting patient outcomes such as survival,^{6,19} time to neutrophil engraftment (TNE) was selected as the *patient* outcome variable for this exploratory analysis. Using patient and caregiver data (controlling for patient medical variables), we hypothesized that lower caregiver distress and better caregiver subjective and objective sleep patterns (assessed prior to patients' engraftment) would be related to reduced TNE in the corresponding patients.

Methods

Participants

This secondary exploratory analysis represents information from caregivers and their Allo-HSCT patients collected prior to transplantation. The caregivers were recruited for participation in a randomized clinical trial of a cognitive-behavioral stress management intervention¹⁵. The primary caregiver inclusion criteria included caring (basic home support, transportation, medication management, emotional involvement) for an allo-HSCT patient at least 50% of the time during the first 100 days post-transplant and ability to speak/read English. Other participant criteria can be seen elsewhere¹⁵. Because caregiver randomization occurred after collecting baseline data (presented herein), any psychological measures were presumably uninfluenced by randomization. 267 caregiver-patient dyads were approached sequentially for study participation sequentially at a private clinic and, of these, 149 dyads were consented. TNE was available from medical records (indicated below) for 136 caregiver-patient dyads (three patients withdrew, four patients passed away prior to engraftment and medical record abstraction data were unavailable for six patients). To avoid potential confounding of the timing of caregiver sleep assessment (e.g., well-being improving due to caregiver knowledge of successful engraftment), twelve caregivers who completed sleep assessments following their patients' engraftment were eliminated leaving a final sample size of 124 dyads. All participants provided informed consent and the parent study was approved by the Colorado Multiple Institution Review Board as described elsewhere¹⁵.

Actigraphy

Sleep patterns were measured using multiaxial accelerometer wrist watches (Model GT3X+, Actigraph, Pensacola, FL). Wrist actigraphs were given to caregivers to wear for three consecutive 24-hour periods on their non-dominant arm after which baseline questionnaires were completed. Participants were asked to only take the device off when performing water-related activities (showering, doing dishes). If the accelerometer battery failed or the accelerometer received water damage, this was treated as missing data. Data were manually analyzed using ActiLife Software Version 5.1 (Actigraph, Pensacola, FL) that calculated quantitative information in several domains: wake after sleep onset (WASO), total sleep time, sleep efficiency, and sleep latency. ActiLife uses the Cole-Kripke algorithm²⁰ for computing summary values. In accordance with other actigraphy literature, WASO is defined as the time an individual, on average, is awake after initially falling asleep, total sleep time is the number of hours reported asleep, sleep efficiency is the total sleep time divided by the number of hours in bed and, finally, sleep latency is the amount of time that it takes an individual to fall asleep. This actigraphy method has been validated and used to

track circadian rhythms and sleep patterns in caregivers²¹. A sleep diary inquiring about individuals' daily sleep patterns (time lying down, estimated hours asleep) was completed each morning for three days to cross validate actigraph information.

Self-reported caregiver sleep

The Pittsburgh Sleep Quality Index (PSQI) is a commonly used self-report of sleep quality that assesses sleep latency, sleep efficiency, and sleep duration as component scores. It has adequate reliability and validity with diagnostic sensitivity of 89.6% and specificity of 86.5%²². Total scores ≤ 5 on each component indicate significant sleep difficulty.

Composite distress score

A caregiver composite distress score was created via principal component analysis (PCA¹⁵), which extracted the first principal component from five psychological measures: Perceived Stress Scale²³, the Center for Epidemiological Studies of Depression Scale²⁴, Total Mood Disturbance on the Profile of Mood States²⁵, the State Anxiety Inventory²⁶ and the Impact of Events Scale²⁷. Each of these measures are widely accepted and demonstrate high test-retest reliability with Cronbach's alpha for the full study sample at baseline¹⁷ of .89, .90, .89, .93 and .85 respectively for each of these measures. This composite was selected as a predictor to reduce the number of statistical comparisons (separate from sleep) and to extend its application from prior work¹⁵. A stringent factor score of 0.70 or greater was required for inclusion in the composite²⁸.

TNE

The primary dependent variable was the time from transplant to neutrophil engraftment (TNE) extracted from medical records. TNE (days) was defined as the number of days until the patient retained an absolute neutrophil count (ANC) of greater than 500 cells/ μ L on 3 consecutive days²⁹.

Patient covariates

As noted above, the primary focus of the parent study was caregiver well-being and providing stress management for these caregivers; thus patient information collected was retrospectively extracted from the medical chart. This included basic demographic information, pre-transplant conditioning intensity (categorized by study oncologists as high, medium and low intensity) and patient completed health summary scores (SF-36).

Statistical analyses

All variables were examined for outliers and departures from normality to ensure the appropriate use of parametric statistics. Analyses were conducted using SPSS Version 22 (IBM Corp, Armonk, NY). An independent-samples t-test compared TNE in days to assessments for caregivers whose baseline information was collected before transplant date and assessments and for those whose information was collected on or after transplant date. Patients' TNE in days was modeled using multiple linear regression. In the first block, *patient* variables that have previously been related to TNE⁶ were selected a priori and entered. These included age, sex, pre-treatment conditioning intensity³⁰, Karnofsky

performance status rated by the medical team^{31,32} and patient SF-36 composite well-being score³³. In the second block, patient education, annual income, comorbidity index³⁴, duration of illness, and timing of caregiver sleep assessment (relative to transplant date) were examined through Pearson correlations and included if significantly related to patient TNE ($p < .05$). An independent t-test compared engraftment for HLA match and mismatch. Building upon these established first and second blocks of covariates, separate regressions were conducted with the following as predictors in the final block: 1) actigraph calculations (WASO, total sleep time, sleep efficiency and sleep onset) 2) subjective caregiver sleep quality (PSQI) and 3) caregiver composite distress score. List wise deletion was applied to all models and residuals were evaluated to further confirm homogeneity of variance assumptions. Relationships were considered statistically significant at $\alpha < .05$.

Results

Demographic data

Caregivers were primarily (77%) Caucasian females ($M_{age} = 52.7$; $SD = 12.3$) and patients were primarily (79%) Caucasian males (67%; $M_{age} = 49.2$; $SD = 12.7$) as summarized in Table 1. Mean TNE was 16.84 days ($SD = 6.41$). On average, caregivers completed their sleep assessment 1.88 days ($SD = 9.65$) before patient transplant and 18.72 ($SD = 11.55$) days prior to patient TNE. Additional analyses were conducted to confirm that the timing of caregivers' psychological assessments was not related to patient TNE. First, there was not a significant relationship between caregivers time of assessment and the primary dependent variable, TNE ($r = -.027$; $p = .85$). There was no significant difference in TNE for patients whose caregiver was collected *before* transplant date ($M = 17.33$, $SD = 7.37$) and for patients whose caregiver assessment was collected *on or after* transplant date ($M = 15.58$, $SD = 6.79$); $t(113) = -1.33$, $p = .19$. These results suggest that the timing of caregivers' psychological assessments were unrelated to TNE.

Objective sleep by actigraphy

On average caregivers were awake for 7.17 minutes after sleep onset ($SD = 8.60$ minutes) across the 3 days of assessment. Average sleep efficiency was 84.8% ($SD = 7.37$), average WASO was 73.91 minutes ($SD = 38.9$) and average sleep time was 6.80 hours ($SD = 1.11$; Table 2). Actigraphy data were verified by comparison with the 3-day sleep diaries for sleep efficiency, sleep time, and WASO.

Subjective sleep (PSQI)

Based on the PSQI, caregivers reported sleep disruption. Their total PSQI score ($M = 11.54$; $SD = 2.73$) exceeded the published cutoff of five²². Examination of the components of the PSQI suggested that Sleep Duration and Habitual Sleep Efficiency were atypical such that all caregivers reported the highest possible disturbance in both characteristics ($M = 3.0$; $SD = 0$).

Distress Composite

The distress composite score from the PCA identified one common factor as previously reported¹⁷ which included the Perceived Stress Scale, the Center for Epidemiological

Studies of Depression Scale, Total Mood Disturbance on the Profile of Mood States, the State Anxiety Inventory and the Impact of Events Scale. Each met the factor loading requirement of being above .70. This common factor (termed caregiver distress) was coded such that higher scores indicated *poorer* mental health. Similar to this prior report¹⁵, the five affective measures included in the distress composite were highly correlated with the composite generated from PCA analysis.

Potential covariates

Only two variables evaluated as potential covariates were significantly related to TNE: patient education ($r = -.17$; $p < .05$) and HLA match ($M = 15.96$ days; $SD = 5.17$) vs. mismatch ($M = 19.68$ days; $SD = 10.49$; $t(112) = -2.53$, $p < .05$). Both variables were included in the second block of subsequent regression models described below in addition to the theoretically driven covariates entered into the first block (age, sex, pre-treatment conditioning intensity, patient's Karnofsky rating and patient's SF-36 mental and physical scale scores).

Time to engraftment (TNE) models

Objective sleep—First, objective actigraphy measures of caregiver sleep patterns were evaluated. When sleep parameters (WASO, sleep time, sleep efficiency and sleep onset) were entered separately into the last block of the regression equation (with patient medical variables controlled for in the first two blocks), caregiver sleep efficiency emerged as a highly significant predictor of patient TNE ($\beta = -.34$; $p < .01$; total $R^2 = .26$). Similarly, greater WASO was significantly related to longer TNE ($\beta = .29$; $p < .05$; total $R^2 = .22$); sleep time ($\beta = -.18$ $p = .09$) and sleep onset ($\beta = .023$ $p = .85$) were not significantly related to TNE (Table 2). Additionally, all regression models were re-run controlling for all variables listed under *Potential Covariates* and significant relationships remained. That is, two variables representing poorer caregiver sleep (lower sleep efficiency and more frequent awakening after sleep onset) predicted longer patient TNE.

Subjective sleep—Next, caregivers' subjective ratings of sleep were entered separately into the last block of the regression equation. Overall caregiver subjective sleep quality significantly predicted patient TNE after controlling for significant covariates (standardized $\beta = .22$; $p < .05$; total $R^2 = .21$), such that worse caregiver sleep quality (higher PSQI score) was related to a longer patient TNE. For illustrative purposes, bivariate scatterplots of these significant relationships (caregiver PSQI score, actigraph sleep efficiency and WASO with patient TNE) are presented in Figure 2.

Caregiver distress—Finally, the relationship of caregiver distress to patient TNE was entered into the last block of the regression and was not statistically significant after controlling for the aforementioned covariates (standardized $\beta = .14$ $p = .22$).

Discussion

This study examined caregiver sleep patterns and their relation to TNE, an important clinical outcome for Allo-HSCT patients. In this study, both subjective caregiver self-report of sleep

quality and objective actigraph measurements of sleep (sleep efficiency and wake after sleep onset) were significant predictors of TNE. To our knowledge, this is one of the first reports to relate any aspect of caregiver well-being such as sleep to clinical outcomes of Allo-HSCT patients, despite extant literature highlighting the importance of this dyadic relationship and the caregiver distress³⁵. These findings underscore the peri-transplant period as a particularly sensitive time for examining relations between psychosocial factors of the caregiver since this is a time when additional supportive interventions may impact clinical outcome. Nurses, as the front line of monitoring patient well-being and interacting with caregivers, are well positioned to observe these caregiver-patient dyadic relationships and provide support as needed.

It is important to extend previously published models linking psychosocial factors and patient outcome¹¹ to relationships represented in the patient-caregiver dyad. The model (Figure 1) outlined several variables such as anxiety, depression, and/or sleep that may be particularly relevant within dyads when examining patient outcome. Thus the current study results represent an initial, exploratory, examination of such relationships. Overall caregiver distress was not related to TNE; however, three caregiver sleep variables (subjective sleep quality, wake after sleep onset and sleep efficiency) emerged as significant predictors of patient TNE. All of these relationships were in the hypothesized direction. This suggests a convergence of objective and subjective measurements as being related to patient outcome. The caregiver sleep variables measured in the current study demonstrated some statistical overlap that is worth highlighting. Each were entered as separate predictors in regression equations to avoid multicollinearity, and, indeed, sleep onset latency was significantly correlated with subjective sleep quality ($r = 0.37$; $p < .05$) but not significantly correlated with wake after sleep onset ($r = -0.09$; $p = .38$). This first relationship is consistent, albeit to a lesser degree, with another report reporting of a correlation of 0.45 between objective and subjective measures of sleep³⁶. However, the overall lack of a significant relationship between subject reports of sleep quality (PSQI) and the actigraphy data is consistent with other literature suggesting variable statistical overlap between these seemingly similar constructs³⁷. This could partially explain that subjective report of sleep quality (PSQI) was noticeably worse than actigraphy measures, which were within ranges comparable to other reports of caregiver actigraphy^{38,39}. Nevertheless, it is encouraging that both objective actigraphy measurements and subjective reports of sleep quality of caregivers prior to transplant were both significantly related to patient outcomes. Future work may build on extending the study of dyadic constructs – and variables that are likely shared within dyads such as caregiver sleep – by measuring variable that we were unable to collect in these secondary analyses. A plausible explanation of the current study is that caregiver sleep disturbance *mirrors* patient sleep disturbance¹. While caregivers' subjective sleep ratings were anchored to the time prior to patient's transplant, the majority of the caregivers' actigraphy assessments occurred during patients' hospitalization (1.88 days prior transplant on average). Not surprisingly, patients' sleep is significantly worse during hospitalization⁴⁰, which may create sleep disturbance in the caregiver. Prior work has noted a strong reciprocity in sleep quality between bed partners among cancer patients and their caregivers⁴¹, thus the relationship among sleep quality and TNE may be more fully explained by patient's disturbed sleep. Although 70% of the caregivers were spouses of their

patients in the current study, it is unlikely that these caregivers were bed partners with patients close to the day of transplant when patients were hospitalized (e.g., hospital beds being single beds etc.). However, some caregivers may have disrupted sleep assuming that their patient is not sleeping well in the hospital which may partially explain the significant relationship between caregiver actigraphy assessment and patient TNE. These potential explanations are limited to the data available in this study regarding where (e.g., patient was inpatient versus at home) the caregivers completed their sleep assessments. Future research should assess the context of sleep measurements in greater detail and for a longer period of time. Another potential explanation for these findings is that a well-rested caregiver provides better care for their respective patient, thereby influencing their TNE. Having support from the caregiver and their oversight of care provided during the peri-transplant period may directly benefit the patient. In fact, some data suggest the mere presence of a caregiver during the inpatient stay of an Allo-HSCT patient may relate to important clinical outcomes, such as survival, in the patient. In a retrospective study of 131 Allo-HSCT patients⁴² and in a prospective study of 164 Allo-HSCT patients,⁴³ survival was related to amount of time the patient's caregiver was present with the patient during hospitalization. While the mechanism is unclear for this observation, these data suggest that the presence of a caregiver in the hospital during the HSCT process resulted in improved patient outcome. Of course, the relationship between caregivers and patient outcome may be more complex than simply the presence of a caregiver. The results of the current study suggest one potential contributing caregiver factor (i.e., sleep) in such relationships. Additional examination of the interrelatedness of the caregiver-patient dyad in HSCT, and what variables may be most relevant to patient outcome, is an area for future research.

The present results should be interpreted carefully in light of a number of limitations. First, these observations are based on secondary analysis in which many patient variables including sleep were not available. As noted above, although meta-analyses suggest that psychological distress is related within patient-caregiver dyads¹, future studies must assess patient sleep along with caregiver sleep to accurately measure dyadic sleep quality and potential bidirectional influences on clinical outcomes such as TNE. Studies are under way examining subjective sleep reports in patients and their caregivers. Second, in the current analyses, very little information was collected from the patient. While the patient SF-36 summary scores were entered as covariates in the analyses presented, there are likely additional patient factors (likely biomedical) not captured in the parent study that influence the TNE relationship. Such mediating and moderating factors are important to capture in future studies, and will help identify other contributing factors to the complex relationships examined in current paper. Returning to our conceptual model in Figure 1, the horizontal arrow leading to patient outcome, in the present case TNE, includes many relevant factors such as patient quality of life as well as patient sleep that were not available for these secondary analyses. Finally, this study was limited by only a brief caregiver sleep assessment during the peri-transplant period. A two-week sleep diary and actigraphy assessment has been advocated elsewhere⁴⁴. Assessing sleep for two weeks, albeit more challenging, may uncover subtle individual differences in caregiver sleep patterns that relate to patient outcome(s).

Implications for Practice

The current results highlight the stress that patient-caregivers experience during the peri-transplant period, pointing to this timeframe as a particularly important time in which to provide psychological support. This period might not only be a “window of opportunity”¹² for studying psychological factors and health outcomes, but also may represent a time during which supportive interventions have potential to produce benefits in health outcomes in both the caregiver and their patient. If increased access to behavioral health professionals remains a challenge, nursing staff can continue to support patient-caregivers throughout the transplant period. Prior work has suggested that caregivers demonstrate reduced distress following interventions during the peri-transplant period in the parent study¹⁵; however, whether this intervention improved the sleep patterns that emerged as significant predictors in the current report remains for future analysis. Targeting sleep disturbance may be a fruitful direction in designing supportive services with a growing evidence base as effective psychological interventions, such as cognitive behavioral treatment for insomnia⁴⁴. Such services, if interpreted in light of the current results, may have the potential to beneficially impact clinical outcome.

In summary, these secondary analyses found that better sleep characteristics reported by caregivers of Allo-HSCT patients were related to a shorter TNE in patients. Despite numerous reports advocating for the care of the caregiver,^{35,45} the degree to which caregiver well-being impacts patient outcome is a new area of investigation. This study represents an initial step in examining this relationship and the results underscore certain relevant caregiver variables (sleep) worth further study within the conceptual model initially presented (Figure 1). Future research should include contributing factors to the relationships observed in this study such as more comprehensive measure of patients’ medical status and capturing more details of the environment in which sleep measurements are taken. Lastly, attention to caregivers’ psychological well-being should be prioritized, particularly including sleep quality, throughout the Allo-HSCT process in the hopes of providing better supportive care for the patient and caregiver. Nursing staff caring for Allo-HSCT patients, and assisting their families, are well positioned to monitor these behavioral manifestations and support patient-caregiver dyads throughout the Allo-HSCT process. The peri-transplant period represents a period of high distress for these dyads in which addressing caregiver distress may, in turn, impact patient outcome in previously unexpected directions.

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Figure 1.

This guiding conceptual framework posits that patient and caregiver well-being overlap significantly and elements of this shared experience may contribute to patient medical outcome. The bidirectional arrow between patient and caregiver well-being represents the reciprocity of the dyad members. Sleep, which was selected as the primary predictor variable of interest in the current study, is emphasized in bold as a proxy for these potential relationships. Patient medical outcome is operationalized as the time to neutrophil engraftment (TNE) for the current study population of stem cell transplant patient-caregiver dyads.

Figure 2.
Bivariate scatterplots of caregivers' subjective sleep quality and objective sleep patterns compared with respective patient time to neutrophil engraftment

Table 1

Demographic Characteristics of Patients and Caregivers

Characteristics	Patients (n = 124)	Caregivers (n = 124)
Age, mean (SD), yr	49.17 (12.7)	52.74 (12.3)
Sex, No. (%)		
Female	39 (31.5)	96 (77.4)
Male	83 (66.9)	28 (22.6)
Marital Status, No. (%)		
Single	15 (12.1)	4 (3.2)
Married	89 (71.8)	112 (90.3)
Divorced	3 (2.4)	6 (4.8)
Widowed	2 (1.6)	2 (1.6)
Ethnicity, No. (%)		
Caucasian	99 (79.8)	115 (92.7)
African-American	2 (1.6)	1 (0.8)
Hispanic	5 (4.0)	5 (4.0)
Asian	0 (0.0)	1 (0.8)
Annual Income, mean (SD) ^a	6.69 (3.06)	7.33 (2.76)
Education, mean (SD) ^b	4.45 (1.38)	4.76 (1.21)
Karnofsky Rating, mean (SD)	92.42 (7.14)	
Duration of Illness, mean (SD), months	24.64 (34.82)	
Comorbidity Index Rating, mean (SD)	2.15 (1.60)	
Patient Category		
Diagnosis, No. (%)		
Acute Lymphoblastic Anemia	10 (8.1)	
Acute Myeloid Leukemia	48 (38.7)	
Hodgkins Lymphoma	3 (2.4)	
Mucopolysaccharidoses	5 (4.0)	
Non-hodgkins Lymphoma	17 (13.7)	
Chronic Lymphocytic Leukemia	7 (5.6)	

Characteristics	Patients (n = 124)	Caregivers (n = 124)
Chronic Myelogenous Leukemia	5 (4.0)	
Severe Aplastic Anemia	1 (0.8)	
Myelodysplastic Syndrome	18 (14.5)	
Multiple Myeloma	6 (4.8)	
Myeloproliferative Neoplasm	1 (0.8)	
Other	3 (2.4)	
Transplant Source, No. (%)		
Matched Sibling	42 (33.9)	
Matched Other	1 (0.8)	
Matched unrelated	54 (43.5)	
Mismatch relative	1 (0.8)	
HLA mismatched	24 (19.4)	
Cord	1 (0.8)	
First Transplant Experience, No. (%)	103 (83.1)	
Second/Third Transplant, No. (%)	17 (13.7)/4(3.2)	
Pre-treatment Intensity, No. (%)		
Reduced	33 (26.6)	
Mid	23 (18.5)	
Full	66 (53.2)	

^aLess than \$5,000 = 1; \$5,000–9,999 = 2; \$10,000 – 14,999 = 3; \$15,000 – 24,999 = 4; \$25,000 – 34,999 = 5; \$35,000 – 44,999 = 6; \$45,000 – 54,999 = 7; \$55,000 – 64,999 = 8; \$65,000 – 74,999 = 9; Greater than \$75,000 = 10

^bGrade school or less = 1; Some high school or technical school = 2; High school or technical school graduate = 3; Some college = 4; College graduate = 5; Some graduate or professional school after college = 6; Completed advance degree = 7

Multiple Regressions of Caregivers' Actigraphy, PSQI Scores, Overall Distress and Actigraph Component Score Predicting Patients' Time to Engraftment After Controlling for Patient Variables.

Table 2

	Standardized β	b (standard error)	t	p	R ² (R ²)
Objective Sleep Assessment					
Wake After Sleep Onset (WASO; <i>M</i> = 73.91; <i>SD</i> = 38.9)	.29	.040 (.016)	2.53	.014	.22 (.075)
Total Sleep Time (<i>M</i> = 6.80; <i>SD</i> = 1.11)	-.17	-.014 (.010)	-1.50	.14	.17 (.028)
Sleep Efficiency (<i>M</i> = 84.77; <i>SD</i> =7.37)	-.35	-.26 (.078)	-3.25	.002	.26 (.12)
Sleep Latency (<i>M</i> =7.17; <i>SD</i> = 8.60)	.023	.015 (.078)	.19	.85	.14 (.00)
Subjective Well-being					
Overall PSQI Score (<i>M</i> = 11.54; <i>SD</i> =)	.22	.51 (.24)	2.12	.037	.21 (.045)
Overall Distress (<i>M</i> = .022; <i>SD</i> = .97)	.14	.89 (.71)	1.25	.22	.20 (.017)