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Sleep Quality Following Hematopoietic Stem Cell Transplantation: Longitudinal Trajectories and Biobehavioral Correlates

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Abstract

The present study examined changes in sleep quality following hematopoietic stem cell transplantation (HSCT) and investigated associations with biobehavioral factors. Individuals undergoing HSCT for hematologic malignancies (N=228) completed measures of sleep quality and psychological symptoms pre-transplant and 1, 3, 6, and 12 months post-transplant. Circulating inflammatory cytokines (IL-6, TNF-α) were also assessed. Sleep quality was poorest at one month post-transplant, improving and remaining relatively stable after 3 months post-transplant. However, approximately half of participants continued to experience significant sleep disturbance at 6 and 12 months post-transplant. Mixed-effects linear regression models indicated that depression and anxiety were associated with poorer sleep quality, while psychological well-being was associated with better sleep. Higher circulating levels of IL-6 were also linked with poorer sleep. Subject-level fixed effects models demonstrated that among individual participants, changes in depression, anxiety, and psychological well-being were associated with corresponding changes in sleep after covarying for the effects of time since transplant. Sleep disturbance was most severe when depression and anxiety were greatest, and psychological well-being was lowest. Findings

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indicate that sleep disturbance is a persistent problem during the year following HSCT. Patients experiencing depression or anxiety and those with elevated inflammation may be at particular risk for poor sleep.

Keywords

cancer; hematopoietic stem cell transplantation; sleep; depression; anxiety; inflammation

Individuals undergoing hematopoietic stem cell transplant (HSCT) experience significant deficits in quality of life that may persist months or even years after HSCT.[1–3] While sleep disturbance has not been a focus of most quality-of-life investigations in this patient population, there is accumulating evidence that HSCT recipients experience significant sleep concerns following transplant.[4–6] For example, in one of the only studies to focus primarily on sleep concerns of HSCT patients, Andrykowski and colleagues found that approximately one-half to two-thirds of long-term survivors experienced persistent disturbances in energy and sleep, with up to 20% of patients endorsing moderate to severe symptoms.[7]

During the acute period following HSCT, Rischer and colleagues found that sleep worsened during the initial month following transplant and improved by 100 days post-transplant.[8] Difficulty falling asleep and maintaining sleep, along with non-restorative sleep, were the most prominent sleep-related complaints. Although the research was limited by a small sample size, this was one of few studies to use a prospective, longitudinal design to track changes in sleep over time. We sought to build upon these findings by examining changes in sleep disturbance in a larger sample of HSCT patients and extending the follow-up beyond 100 days post-transplant.

Another objective was to investigate biological and behavioral factors associated with sleep problems, which has not been a focus of prior reports. Patients undergoing the demanding and stressful experience of HSCT commonly experience psychological distress, including both depression and anxiety.[9–12] It is already known that depression and anxiety are associated with disrupted sleep,[13–18] but this link has not been studied in HSCT recipients. We therefore examined the extent to which greater psychological distress, including symptoms of anxiety and depression, may be linked with poor sleep.

Emerging literature also indicates that inflammation may adversely affect sleep. Pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α), activate neural pathways associated with the withdrawal and conservation of energy, evoking behavioral and mood responses including fatigue, depression, and sleep disturbance.[19] Immunomodulatory therapies and administered cytokines affect sleep architecture and duration.[20] The associations between proinflammatory activity and sleep disturbance have been documented among cancer populations; for example, poor sleep quality has been linked to IL-6, IL-1RA, and TNF-α levels in breast and prostate cancer patients, although the relationships are not always consistent.[21, 22] A recent study of allogeneic HSCT recipients found an association between IL-6 and treatment side effects, including poor sleep quality.[23] While intriguing, this paper focused more generally on side effects and used a single question to assess sleep quality. Relationships between

inflammation and sleep have not been well-studied among HSCT patients and may be a particular problem because of numerous factors that cause elevated and prolonged inflammation post-HSCT, including tissue injury from conditioning therapy, infections, and graft-versus-host disease. Therefore, we also examined the extent to which blood levels of proinflammatory cytokines in systemic circulation were associated with poor sleep quality.

In sum, the present study had two primary aims. First, we investigated the prevalence and severity of poor sleep quality during the twelve months following transplant. We conducted a comprehensive assessment of dimensions of sleep quality to determine which sleep domains are most problematic and tracked changes in sleep quality over time. The second aim was to investigate psychological and biological factors related to sleep difficulty. Given the known contributions of depression and anxiety to sleep problems in other populations and their high prevalence among HSCT recipients, we hypothesized that patients with greater depression and anxiety symptoms would experience poorer sleep quality while a sense of psychological well-being would be a protective factor. Moreover, because of the well-documented relationships between inflammation and sleep impairment, and elevated levels of inflammatory cytokines in the setting of HSCT, we hypothesized that patients with higher levels of inflammatory cytokines would experience poorer sleep quality. In addition to examining participant differences in these biobehavioral factors, we took advantage of our longitudinal design to determine whether changes in psychological symptoms and inflammation within individual participants over the study period were associated with corresponding changes in sleep quality.

Methods

Participants

The study sample included 228 adults who underwent HSCT at the University of Wisconsin Carbone Cancer Center for treatment of a hematologic disease. Participants were part of a larger, IRB-approved study examining psychological predictors of post-transplant recovery. The study enrolled 59.3% of eligible patients at our institution. A common reason for non-enrollment was the patient starting the transplant regimen before study personnel were aware of eligibility. Of those approached for the study, approximately 80% enrolled. The most commonly stated reasons for declining participation were not having enough time, feeling overwhelmed, or feeling too unwell.

Data from participants who completed the pre-transplant assessment and at least one post-transplant assessment were included in the analyses (N = 228). Due to study attrition, missing data, or mortality, data were available from fewer patients at the 1 (96%), 3 (89%), 6 (82%), and 12 (78%) month follow-up assessments. Known reasons for attrition were death (n = 25) and declining to continue participation (n = 2). Those enrolled were a mean of 51 years of age (range: 19–74) at the time of transplant. The sample included both autologous (n = 128) and allogeneic (n = 100) transplant recipients. Additional demographic and medical characteristics are detailed in Tables 1 and 2.

Procedures

Individuals who agreed to participate provided informed consent and completed study assessments prior to transplant and approximately 1, 3, 6, and 12 months post-transplant. Blood samples were also obtained for a subset of participants at all assessment points except the 12-month follow-up.

Measures

Sleep Quality—Participants completed the 21-item Pittsburgh Sleep Quality Inventory (PSQI) at each time point. The PSQI assesses 7 domains of sleep quality: subjective sleep quality, latency, duration, sleep efficiency (calculated by participant report of time spent asleep in relation to report of time spent in bed), nighttime disturbance, sleep medication use, and daytime dysfunction.[24] The PSQI global score is the sum of the seven domains and ranges from 0 to 21, with higher scores indicating poorer sleep quality. PSQI global scores greater than 5 indicate poor sleep quality.[24] However, others have proposed a cut score of 8 for significantly ill populations.[25] The PSQI has also been found to be a reliable measure in cancer populations, with a reliability coefficient of $\alpha = .73$ in the present study.[25]

Psychological symptoms—Participants completed the 64-item Inventory of Depression and Anxiety Symptoms (IDAS) at each time point. This scale measures symptoms of depression and anxiety as well as general psychological well-being.[26] We focused on dysphoria, a measure of cognitive and affective depression symptoms; (e.g., “I felt depressed;” “I blamed myself for things”), panic/somatic anxiety (e.g., “I was trembling or shaking;” “My heart was racing or pounding”) and psychological well-being scales (e.g., “I felt optimistic;” “I felt that I had a lot to look forward to”). The IDAS has several advantages over other depression and anxiety measures, including superior ability to discriminate between depression and anxiety symptoms, content that more closely reflects DSM criteria, the ability to examine symptom dimensions, and a quick and efficient format. Moreover, the IDAS is particularly well-suited for populations where medical symptoms may overlap with depression and anxiety symptoms.[27, 28] IDAS scores also show strong correlations with structured interview diagnoses of depression and anxiety.[26] In the present sample, the IDAS scales demonstrated excellent reliability (α-coefficients ranged from .85–.90).

Cytokines—Peripheral blood was obtained from a subsample of participants to assess circulating levels of IL-6 and TNF-α. Cytokine assessments were added to the study protocol later, and therefore are available for the most recently enrolled participants (n = 91). IL-6 and TNF-α are potent inflammatory cytokines that have been linked to quality of life measures, including sleep, among healthy populations as well as cancer patients.[29–31]

Blood samples were centrifuged and separated plasma frozen at −80°C. Enzyme-Linked ImmunoSorbent Assay (ELISA) was used to assess cytokine levels using standard high sensitivity kits (R&D Diagnostics, Minneapolis, MN). For all cytokine analyses, samples were classified as falling into low/normal range versus elevated on the basis of established field-relevant values and reference ranges from the manufacturer.[32] Cut-offs for elevated scores were as follows: above 3 pg/mL for IL-6 and 1.41 pg/mL for TNF-α. At the four

assessment points, 12–32% of patients exceeded the cut-off for elevated IL-6, and 25–50% exceeded the cut-off for TNF-α.

Statistical analyses

StataSE statistical package was used to analyze data. All statistical tests were two-sided, and results considered significant at $p < 0.05$. Sleep was treated as a continuous variable in all analyses. Repeated measures ANOVA was used to examine changes in sleep quality across the five study time points. Significant temporal changes were explored with post-hoc pairwise comparisons between time points.

Relationships between time-varying biobehavioral factors (psychological symptoms and circulating cytokine levels) and time-varying global sleep quality were assessed with mixed-effects and fixed-effects regression models. Separate models were run for each psychological measure or cytokine. Several potential covariates were considered for inclusion in the models, including age, sex, graft type (allogeneic versus autologous transplant), conditioning regimen (myeloablative versus nonmyeloablative), total body irradiation (TBI), initial diagnosis, disease status (remission versus recurrence/progression), steroid use, and occurrence of infections. Women, younger patients, and those who had experienced disease recurrence or progression reported significantly poorer sleep quality at some post-transplant time points (p values < 0.05), and steroid use was marginally linked to sleep quality at some time points (p values < 0.10). Therefore, sex, age, disease status, and steroid use were included as covariates in subsequent analyses. Other demographic and clinical variables were not associated with sleep quality. However, graft type and conditioning regimen were included as a conservative step given the different side effect profiles and recovery time anticipated with different treatment regimens.

Mixed-effects linear regression models examined relationships between participant differences in biobehavioral variables and sleep quality. All models included time since transplant entered as a factor variable and adjusted for between-subjects covariates, including sex, age, graft type, and conditioning regimen, as well as time-varying covariates, including steroid use and disease status. Time-varying psychological predictors were standardized based on 12-month post-transplant means and standard deviations before being entered in the models to improve interpretability of the model coefficients. Subject-level fixed effects models were then employed to determine the extent to which changes in psychological symptoms and circulating cytokines within individual participants were associated with corresponding changes in global sleep quality, effectively allowing each participant to act as his/her own control. These models also included time since transplant as a factor variable and time varying-covariates, including steroid use and disease status. While not a primary study aim, mixed-effects linear regression models were also used to examine relationships between the psychological variables and cytokine levels.

Results

Poor Sleep Quality Prevalence, Severity, and Change Over Time

Table 3 provides descriptive information about the percent of participants who endorsed various response categories for each of the PSQI domains and who fell above global PSQI cut scores. The majority of participants exceeded the standard cut score of 5 at most time points.

Figure 1 illustrates mean global sleep quality scores across the time points, with higher scores indicating poorer sleep quality. Significant changes in global sleep quality were evident over time, $F(4, 778) = 20.87$, $p < 0.001$. Post-hoc comparisons clarified that sleep quality declined significantly from pre-transplant ($M = 6.98$, $SD = 4.11$) to one month post-transplant ($M = 8.11$, $SD = 4.17$) followed by improvement at three months post-transplant ($M = 6.49$, $SD = 3.73$) after which sleep remained relatively stable through six months ($M = 6.18$, $SD = 3.76$) and twelve months post-transplant ($M = 6.07$, $SD = 3.65$). Mean sleep quality scores were poorer than population norms at all time points.[24]

Figure 2 illustrates the trajectory of each sleep quality dimensions over time; these seven dimensions comprise the global sleep quality score. The highest mean scores (indicating poorer sleep) were seen for difficulty staying asleep (nighttime disturbance), followed by difficulty falling asleep (latency), and daytime dysfunction due to sleep disturbance. Sleep duration had the lowest scores (indicating that most patients were sleeping a sufficient number of hours). Significant changes over time were seen in five of the seven sleep domains, including subjective sleep, $F(4, 778) = 10.62$, $p < 0.001$; sleep duration, $F(4, 773) = 9.12$, $p < 0.001$; sleep efficiency, $F(4, 749) = 8.96$, $p < 0.001$; sleep medication use, $F(4, 776) = 15.65$, $p < 0.001$; and daytime dysfunction, $F(4, 781) = 8.85$, $p < 0.001$. Post-hoc comparisons indicated that sleep efficiency, sleep medication use, and daytime dysfunction followed the same temporal trajectory as global sleep quality. Subjective sleep and sleep duration followed a slightly different pattern, with consistently high scores (indicating impairment) at pre-transplant and one month post-transplant, followed by improvement at three months post-transplant. Sleep latency and nighttime disturbance did not significantly change over time, all p values > 0.10.

Psychological Symptoms and Sleep Quality

Mixed-effects linear regression models revealed that participants who reported greater depression and anxiety experienced poorer sleep quality, after covarying for the effects of time since transplant, sex, age, graft type, conditioning regimen, steroid use, and disease status. In contrast, participants who reported greater psychological well-being experienced better sleep quality during the twelve months following transplant. Coefficients, test statistics, and p values are provided in Table 4.

Among individual participants, subject-level fixed effects models indicated that changes in depression and anxiety were associated with corresponding changes in sleep quality, with the most severe disturbances in sleep occurring when depression and anxiety were most elevated. Similarly, changes in psychological well-being were associated with corresponding changes in sleep quality, with the most severe disturbances in sleep occurring when

psychological well-being was lowest. These relationships were seen after accounting for the effects of time since transplant, steroid use, and disease status. Coefficients, test statistics, and *p* values are provided in Table 4.

Circulating Cytokine Levels and Sleep Quality

Mixed-effects linear regression models revealed that participants with elevated levels of IL-6 reported poorer sleep quality across all assessment points through six months post-transplant as compared to those with low IL-6. Subject-level fixed effects models showed that changes in levels of IL-6 within individual participants were not significantly associated with corresponding changes in sleep quality. TNF-α was not associated with sleep quality. Coefficients, test statistics, and *p* values are provided in Table 4.

We also examined whether psychological indices (depression, anxiety, well-being) were associated with IL-6 or TNF-α. No significant relationships were seen between the psychological variables and cytokines, all *p* values > 0.10.

Discussion

Our results indicate that patients undergoing HSCT experience significant disturbances in sleep during the twelve months following transplant. 69% of HSCT recipients report poor sleep quality during early post-transplant recovery, with 48% continuing to report moderate to severe disturbances at twelve months post-transplant. Consistent with prior research, the most problematic domains were difficulty falling asleep and awakening during the night.[5, 8]

Sleep quality was evaluated at specific milestones in the post-HSCT recovery process. A consistent pattern of changes in sleep quality was evident from pre- to post-transplant and during the year following transplant. Sleep quality was poorest at one month post-transplant, at which point most patients are typically still experiencing treatment-related side-effects and complications of infections.[33] Sleep quality returned to pre-transplant levels by three months post-transplant, a clinical milestone at which disease outcomes are evaluated.[33, 34] Sleep quality stabilized by six months post-transplant and remained stable through twelve months post-transplant which represent important transitional points in the recovery process when patients may be returning to work and resuming more normal routines, assuming a good HSCT outcome.[35, 36] This overall pattern of change was seen across five of the seven domains of sleep quality as well as for global sleep, and likely reflects the effects of conditioning therapy, immunosuppression, medications, long hospital stays, stress, and adverse physical side-effects of the intensive therapeutic regimen.

The temporal changes in global sleep observed are consistent with Rischer and colleagues and indicate that sleep disturbances return to pre-transplant levels by three months post-transplant.[8] However, we extend these prior findings to show that approximately half of participants continued to show persistently poorer sleep quality at six and twelve months post-transplant. Our results indicate that patients had impaired sleep both immediately prior to and following transplant and suggest that without intervention, many HSCT survivors are at risk for persistent sleep problems. Sleep disturbances such as insomnia increase risk for psychiatric disorders,[37, 38] comorbidities such as cardiovascular disease and diabetes,[39] and

mortality;[40] thus, findings have important clinical implications in placing HSCT recipients at risk for more challenged short- and long-term recovery and overall health.

This study is the first to examine potential psychological and biological underpinnings of sleep disturbance following HSCT. Consistent with initial hypotheses, our data suggest that patients who report greater depression and anxiety symptoms may be more at risk for sleep difficulties during the twelve months following transplant. In contrast, a sense of psychological well-being appears to be protective, with patients who report greater psychological well-being experiencing less sleep difficulty. The same pattern of relationships was seen in examining changes in depression, anxiety, and well-being within individual participants using a within-subjects analysis that capitalized on the longitudinal study design and multiple assessment points. Here we saw that for individual participants, sleep disturbance was worst when anxiety and depression were most elevated, after adjusting for the effects of time since transplant. Findings also highlight the importance of a potentially protective psychological factor, having a sense of well-being. There is growing interest in measures of well-being among cancer survivors,[9] and our results suggest that further attention to these protective factors may be an important avenue for assisting transplant recipients during the recovery process.

Participants who had elevated levels of IL-6 in systemic circulation reported greater sleep disturbance during the six months following transplant as compared to those with normal IL-6 levels. However, changes over time in IL-6 within individual participants from elevated to normal or vice-versa were not associated with changes in sleep, after accounting for the effects of time since transplant. This may have been due to the relative stability in IL-6 levels for most participants. Circulating levels of TNF-α were not associated with sleep disturbance. This study is the first that we are aware of to examine relationships between inflammatory markers and a comprehensive measure of sleep disturbance among HSCT recipients. Findings build upon a prior report by Wang and colleagues which found an association between HSCT symptoms and IL-6 during the initial month following transplant, showing that relationships between inflammation and sleep disturbance in particular can persist beyond the acute recovery period through six months post-transplant.[23] Inflammation related to tissue injury from conditioning regimens, the development of graft-versus-host disease, or infections may exacerbate sleep disturbance following HSCT. The lack of a relationship between sleep and TNF-α levels is consistent with prior literature, which has generally found IL-6 to be a more sensitive biomarker when examining relationships with behavioral factors such as sleep.[23, 41] TNF-α levels may not have been predictive because elevations may have been more transient and therefore less likely to have an impact. It is known that TNF-α is a very fast-responding cytokine, which tends to return to lower basal levels quickly, except in extreme inflammatory conditions such as sepsis.[41, 42]

The current study is one of the first to use a prospective, longitudinal design to evaluate changes in sleep quality over time and sleep disturbance both pre- and post-transplant. This approach enabled us to examine both the effects of individual differences in psychological indices and inflammatory markers but also the extent to which changes in sleep tracked changes in these measures over time within participants. Given that the patients were

undergoing intensive treatments for potentially life-threatening cancers, there were some restrictions and limitations, including reliance on self-report assessments of sleep quality, rather than clinical diagnoses of insomnia. Future studies should also consider other measures of sleep-wake disturbance, such as wrist actigraphy or polysomnography. In addition, our capacity to generalize the conclusions to other populations is limited. Given the patients seen by our cancer center, there was not a wide range of racial/ethnic diversity. Finally, this is an observational study relying on correlations, and therefore we cannot determine with certainty the direction of the effects or causal mechanisms. While our analyses used biobehavioral factors as the predictors in the models, sleep disturbance may in turn exacerbate depression and anxiety and may even alter circulating IL-6.[19] Interventional study designs could help to tease apart the likely complex, bidirectional relationships.

While survival rates have increased over the course of the previous decade, HSCT patients remain at risk for a host of medical and quality-of-life complications. Diminished sleep quality is a significant and persistent problem that can exacerbate other quality-of-life concerns and may even contribute to morbidity and mortality. The risk for sleep problems is highest in the early recovery period, and individuals with high levels of psychological distress and inflammation may be at greatest risk, highlighting important time points and targets for both screening and behavioral or pharmacological interventions targeting sleep concerns. The National Comprehensive Cancer Network Distress Thermometer is frequently employed in cancer centers and includes items pertaining to sleep, depression, and anxiety, making this a useful initial screening tool.[43] Other distress or depression screeners could also be utilized. With regard to interventions, while sleep medications are commonly employed, non-medication strategies may be more ideal given their efficacy, lack of side effects, and growing evidence base in cancer populations. Cognitive-behavioral therapy for insomnia[44] and bright light therapy for circadian rhythm disturbances[45] are empirically supported treatments that are particularly promising for the HSCT setting. In addition to approaches focusing directly on sleep, interventions that alleviate anxiety and depression and promote psychological well-being may be important to consider as well.

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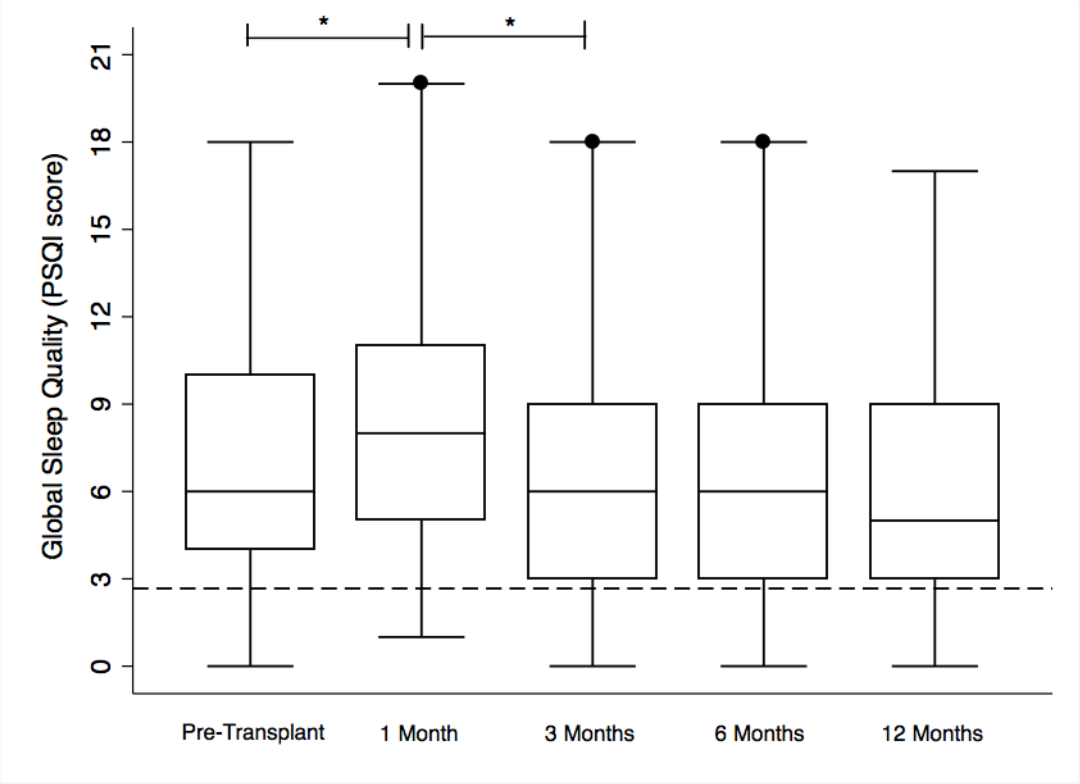

Figure 1.

Distribution of global sleep quality from pre-transplant through twelve months post-transplant. Higher scores indicate poorer sleep quality. The box represents the lower and upper quartiles and the middle band represents the 50th percentile. The whiskers represent the lowest and highest datum within 1.5 interquartile range of the lower and upper quartiles. Data falling outside this range are represented with a dot. The dashed line represents the global sleep quality population norm (M=2.67).[24] Significant changes in global sleep quality were evident over time, $F(4, 778) = 20.87$, $p < 0.001$. Post hoc comparisons clarified that sleep quality declined from pre-transplant to one month post-transplant followed by improvement at three months post-transplant, after which sleep remained relatively stable through six and twelve months post-transplant. Significant changes are denoted with an asterisk.

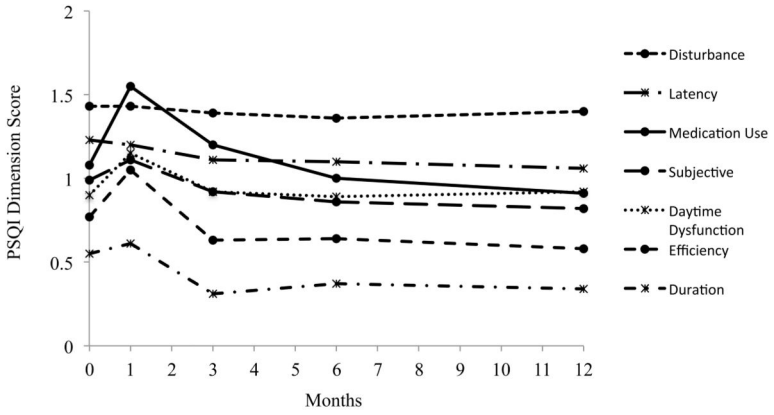

Figure 2.

Mean scores on dimensions of sleep quality from pre-transplant through twelve months post-transplant. All dimensions are scored on a 0–3 scale, with higher scores indicating poorer sleep quality. Participants completed the first assessment prior to transplant, represented here as 0 months post-transplant. Dimensions include subjective sleep, latency, duration, sleep efficiency, nighttime disturbance, sleep medication use, and daytime dysfunction. There were significant changes in five of the seven sleep domains including: subjective sleep, $F(4, 778) = 10.62$, $p < 0.001$; sleep duration, $F(4, 773) = 9.12$, $p < 0.001$; sleep efficiency, $F(4, 749) = 8.96$, $p < 0.001$; sleep medication use, $F(4, 776) = 15.65$, $p < 0.001$; and daytime dysfunction, $F(4, 781) = 8.85$, $p < 0.001$. Post hoc comparisons indicated that sleep efficiency, sleep medication use, and daytime dysfunction followed the same temporal trajectory as global sleep quality. Subjective sleep and sleep duration followed a slightly different pattern, with consistently high scores (indicating impairment) at pre-transplant and one month post-transplant, followed by improvement at three months post-transplant.

Table 1

Demographics at Study Enrollment (N = 228)

Patient Characteristics	%	n
Gender		
Male	60.5	138
Female	39.5	90
Ethnicity		
Caucasian	96.5	220
Native American	1.3	3
African American	0.9	2
Latino/Hispanic	0.9	2
Asian American	0.0	0
Unknown	0.4	1
Relationship Status		
Married or Living with partner	82.5	188
Single	8.8	20
Divorced or Separated	7.0	16
Widowed	1.7	4
Completed Education		
Less than 12 years	4.4	10
High School Graduate	28.5	65
Some College or Trade School	25.4	58
College Graduate	25.9	59
Post-Graduate Degree	15.4	35
Unknown	0.4	1
Employment		
Employed Full or Part time	41.3	94
Disabled	30.7	70
Retired	21.5	49
Homemaker	4.4	10
Unemployed	0.4	1
Student	0.4	1
Unknown	1.3	3
Income		
<25,000	13.6	31
25,001–55,000	29.0	66
55,001–85,000	27.6	63
>85,000	24.1	55
Unknown	5.7	13

Table 2

Disease and Treatment Characteristics (N = 228)

Patient Characteristics	%	n
Graft Type		
Autologous	**56.1**	**128**
Allogeneic	**43.9**	**100**
Myeloablative	29.4	67
Matched Sibling Donor	13.6	31
Matched Unrelated Donor	14.9	34
Cord Blood	0.9	2
Nonmyeloablative	14.5	33
Matched Sibling Donor	6.6	15
Matched Unrelated Donor	6.1	14
Cord Blood	1.8	4
Diagnosis		
Leukemias	**33.8**	**77**
MDS	18.2	14
AML	48.0	37
ALL	26.0	20
CML	2.6	2
CLL	5.2	4
Lymphomas	**32.9**	**75**
Hodgkin	26.7	20
Non Hodgkin	73.3	55
Multiple Myeloma	**33.3**	**76**

Table 3

Prevalence of poor sleep quality

	Time points				
	Pre-Transplant *n* = 223	**One Month Post- Transplant *n* = 219**	**Three Months Post- Transplant *n* = 203**	**Six Months Post- Transplant *n* = 188**	**Twelve Months Post-Transplant *n* = 177**
Sleep Dimensions	**%**	**%**	**%**	**%**	**%**
Global Sleep Quality					
Good (≤5)	44.0	31.1	44.3	47.3	52.0
Poor (>5)	56.0	68.9	55.7	52.7	48.0
Poor (>8)	35.0	41.1	29.6	25.5	26.0
Subjective Sleep					
Very Good	24.2	14.2	25.1	26.6	29.9
Fairly Good	54.7	62.1	60.1	62.8	58.2
Fairly Bad	19.3	21.9	12.8	9.0	11.9
Very Bad	1.8	1.8	2.0	1.6	0.0
Sleep Latency (min)					
0–15	25.0	29.8	31.0	32.6	33.5
16–30	40.9	35.8	40.4	36.4	38.1
31–60	20.5	19.3	14.8	19.3	17.6
>60	13.6	15.1	13.8	11.8	10.8
Sleep Duration (hrs)					
<5	5.4	6.4	0.5	2.1	2.3
5–6	9.5	11.0	6.4	6.4	5.2
>6–7	19.4	19.7	16.3	17.5	16.2
>7	65.8	62.8	76.9	74.1	76.3
Sleep Efficiency (%)					
<65	11.7	21.1	7.1	8.6	5.9
64–74	10.8	10.3	8.2	8.6	9.4
75–85	20.6	21.1	25.5	20.9	21.8
>85	57.0	47.4	59.2	62.0	62.9
Nighttime Disturbance					

	Time points				
	Pre-Transplant *n* = 223	**One Month Post- Transplant *n* = 219**	**Three Months Post- Transplant *n* = 203**	**Six Months Post- Transplant *n* = 188**	**Twelve Months Post-Transplant *n* = 177**
Sleep Dimensions	**%**	**%**	**%**	**%**	**%**
0 times per week	3.6	0.9	3.9	4.3	4.5
<1 times per week	53.4	57.5	57.6	57.5	54.2
1–2 times per week	39.9	39.3	33.5	36.7	37.9
≥3 times per week	3.1	2.3	4.9	1.6	3.4
Daytime Dysfunction					
0 times per week	33.2	18.6	25.1	32.3	29.4
<1 times per week	48.0	52.9	59.6	50.3	52.5
1–2 times per week	14.8	23.5	13.3	13.8	15.3
≥3 times per week	4.0	5.0	2.0	3.7	2.8
Sleep Medication Use					
Yes	47.7	62.6	48.8	42.8	38.4
No	52.3	37.4	51.2	57.2	61.6

Note. Global sleep cutoff score of 5 indicates poor sleep.[23] Global sleep cutoff score of 8 can also been used for seriously ill populations.[24]

Table 4

Associations Between Biobehavioral Factors and Global Sleep Quality (N = 228)

	Mixed-effects models				Fixed-effects models			
Measure	***Coef.***	***SE***	***z***	***p***	***Coef.***	***SE***	***t***	***p***
Anxiety	0.75	0.09	8.48	<0.001	0.53	0.10	5.59	<0.001
Depression	1.24	0.06	20.43	<0.001	1.06	0.07	14.60	<0.001
Well Being	−0.70	0.12	−5.76	<0.001	−0.38	0.14	−2.70	<0.01
IL-6	1.04	0.53	1.99	0.047	0.79	0.60	1.33	0.186
TNFα	−0.45	0.46	−0.99	0.324	−0.49	0.53	−0.92	0.358

Note. A subsample of n = 91 participants were included in the IL-6 and TNFα models which did not include the twelve month post-transplant time point. Separate models were run for each psychological measure or cytokine. Mixed-effects models covaried for time (treated as a factor variable); age, sex, graft type, and conditioning regimen (between-subjects covariates); and steroid use and disease status (time-varying covariates). Fixed effects models covaried for time and time-varying covariates. Psychological symptom scores were standardized before being entered in the model; therefore, coefficients represent the change in mean PSQI score for each one standard deviation increase in psychological symptoms. Cytokine concentrations were coded as elevated or normal; therefore, coefficients represent the difference in PSQI scores for elevated versus normal cytokine levels.