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Sleep quality predicts future mood symptoms in adolescents with bipolar disorder

Michelle E. Stepan[*], **Peter L. Franzen**, **Giana I. Teresi**, **Noelle Rode**, **Tina R. Goldstein**

Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA, United States of America

Abstract

Background: Poor sleep is prevalent in adolescents with bipolar disorder, precedes illness onset, and is associated with worse mood symptoms. We examined interrelationships between sleep quality and mood symptoms in adolescents with bipolar disorder, particularly effects of sleep quality on emergent mood symptoms.

Methods: Adolescents with bipolar disorder participated in a two-year longitudinal treatment study. Sleep quality (Pittsburgh Sleep Quality Index, PSQI) was assessed quarterly during treatment (baseline, 3-, 6-, 9-, 12-month visits) and twice during follow-up (18-, 24-month visits). Mood symptoms (ALIFE Psychiatric Status Ratings) were retrospectively rated weekly by an independent clinician. Lag models tested whether sleep quality predicted next month's mood symptoms and whether mood symptoms predicted future sleep quality.

Results: Adolescents with bipolar disorder had poor sleep quality. Sleep quality initially improved but remained stable thereafter. Worse sleep quality at 6-months predicted worse depression, hypomania, and suicidal ideation the following month. Sleep quality was worse for adolescents who had a suicide attempt during the study compared to those who did not and was worse preceding months with a suicide attempt compared to months without attempts. Alternatively, worse depression predicted worse future sleep quality at baseline, 3-, and 18-months and worse suicidal ideation predicted worse future sleep quality at baseline, 12-, and 18-months.

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[*]Corresponding author at: 3811 O'Hara St., Pittsburgh, PA 15213, United States of America. stepanme@upmc.edu (M.E. Stepan).

Ethical statement

The University of Pittsburgh's Institutional Review Board approved all study procedures (STUDY19060095). Written consent/assent was obtained from all participants and their parents prior to participation in the study. The study was conducted in line with the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

CRediT authorship contribution statement

Michelle E. Stepan: Writing – original draft, Visualization, Formal analysis. **Peter L. Franzen:** Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition, Conceptualization. **Giana I. Teresi:** Writing – review & editing. **Noelle Rode:** Data curation. **Tina R. Goldstein:** Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no conflicts of interest to disclose.

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Limitations: Mood symptoms were rated retrospectively and the PSQI may not capture all dimensions of sleep important for mood symptoms.

Conclusions: Targeted evidence-based sleep treatment in adolescents with bipolar disorder may alleviate sleep problems and have additional benefits on mood symptoms and suicidality risk.

Keywords

Adolescents; Bipolar disorder; Sleep quality; Pittsburgh sleep quality index; Suicidal ideation; Suicide attempts

1. Introduction

Bipolar disorder is a serious recurrent psychiatric condition affecting approximately 1 % (0.4–2.4 %) of the global population (Merikangas et al., 2011; Ferrari et al., 2016; Merikangas and Pato, 2009). Onset of bipolar disorder tends to occur late in adolescence to early adulthood (Merikangas et al., 2011), with earlier age of onset associated with more severe illness (Merikangas et al., 2011) and increased comorbidity (Joslyn et al., 2016). Indeed, the majority of adolescents in the United States with bipolar disorder exhibited severe psychosocial impairment (Merikangas et al., 2010) and youth with bipolar disorder are at high risk for suicide (De Crescenzo et al., 2017). Thus, adolescents with bipolar disorder are particularly vulnerable to negative long-term outcomes and may especially benefit from early intervention and treatment.

Early onset bipolar disorder is typically associated with a more severe illness trajectory, resistance to treatment, and poorer psychosocial functioning (Rucklidge, 2006; Kowatch and DelBello, 2006; Parellada et al., 2017). In particular, depressive symptoms in youth with bipolar disorder are often severe and debilitating, in part due to difficulties with emotion regulation and effective coping strategies (Rucklidge, 2006; Khafif et al., 2021; Dickstein and Leibenluft, 2006; Salazar de Pablo et al., 2020). Furthermore, adolescents with bipolar disorder are at a much greater risk for a suicide attempt compared to other mood disorders and the general population of adolescents (De Crescenzo et al., 2017; Rucklidge, 2006). While several risk factors for suicidal behavior have been identified, many are not modifiable (e.g., prior history of trauma, family history of bipolar disorder) or do not fully explain fluctuations in depressive symptoms that occur throughout the disorder trajectory. Therefore, it is critical to identify novel modifiable risk factors for bipolar disorder symptomology in youths to improve quality of life.

Poor sleep quality may be an important risk factor for bipolar disorder, particularly during the vulnerable period of adolescence. Due to a number of biopsychosocial factors, sleep undergoes dramatic alterations during adolescence, typically resulting in later sleep timing, shorter sleep duration, more irregular sleep patterns, and increasing insomnia and worsening sleep quality (Illingworth, 2020; Carskadon, 2011; Crowley et al., 2018). Moreover, poor sleep is considered a transdiagnostic risk factor for psychiatric illness (Harvey et al., 2011) and may be a practical, modifiable target to improve a range of symptoms associated with bipolar disorder. Indeed, Interpersonal and Social Rhythm Therapy (Frank, 2007), which aims to regularize rhythms and improve sleep, has shown efficacy in adults (Frank et

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al., 2005; Miklowitz et al., 2007; Goldstein et al., 2018; Hlastala et al., 2010), further implicating sleep as a possible mechanism of mood instability in bipolar disorder.

Specifically, poor sleep often precedes the onset of bipolar disorder. Two prospective 10-year long longitudinal studies, one in children at high risk for bipolar disorder and the other in psychiatrically healthy adolescents, found that decreased and disturbed sleep in youth increased risk for developing bipolar disorder (Ritter et al., 2015; Shaw et al., 2005). Retrospective reports corroborate these findings, indicating that childhood insomnia symptoms were commonly reported in individuals who later developed bipolar disorder (Egeland et al., 2000; Lish et al., 1994). Poor sleep, in fact, may be one of the earliest and most common prodromes of bipolar disorder (Lish et al., 1994; Duffy et al., 2010; Sierra et al., 2007).

Furthermore, poor sleep is quite pervasive throughout the disorder trajectory and persists even during periods of euthymia. Poor sleep and symptoms of insomnia are widely reported in children and adolescents with bipolar disorder (Harvey, 2009). Youth with bipolar disorder and a comorbid sleep disorder were at a heightened risk for suicide (Stanley et al., 2017) and large changes in sleep in adults with bipolar disorder signal impending changes in mood the following day (Bauer et al., 2006). Euthymic adults with bipolar disorder also exhibited poorer and more unstable sleep patterns, when measured using self-report or actigraphy, compared to healthy controls (Cretu et al., 2016; Millar et al., 2004; Harvey et al., 2005), and worse subjective sleep quality was associated with worse subsyndromal depression (Cretu et al., 2016). Furthermore, euthymic adults with bipolar disorder classified as poor sleepers had a shorter time to any mood episode recurrence even when controlling for subsyndromal mood symptoms (Cretu et al., 2016). Taken together, evidence suggests that poor sleep may be a contributing factor in the onset, progression, and recurrence of bipolar disorder.

However, the majority of studies linking poor sleep to mood symptoms have been conducted in adults with bipolar disorder. However, the worsening of sleep during adolescence makes this a particularly relevant developmental window to examine sleep changes in relation to bipolar disorder. Specifically, understanding the interrelationships between sleep and mood symptoms, such as depression and suicidality, in adolescents with bipolar disorder is critical for intervention and treatment efforts. In the current study, we recruited adolescents with bipolar disorder who were enrolled in a larger two year longitudinal randomized controlled trial comparing Dialectical Behavior Therapy with pharmacotherapy (DBT) to Standard of Care psychotherapy with pharmacotherapy (SOC). Sleep quality and mood symptoms were repeatedly assessed, which allowed us to examine complex interrelationships between the two, with a specific focus on the impact of sleep quality on emergent mood symptoms. A sample of healthy controls were also recruited as part of the larger trial to help characterize the sample of adolescents with bipolar disorder, which included collecting baseline assessments.

Our primary aim was to examine how sleep quality influenced subsequent mood symptoms in adolescents with bipolar disorder. We hypothesized that adolescents with poorer sleep quality would endorse worse subsequent mood symptom severity than adolescents with

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better sleep quality. A secondary aim was to examine the inverse relationship—whether mood symptom severity predicted subsequent sleep quality. It has long been postulated that the link between sleep and mood is bidirectional, such that poor sleep leads to worse mood, and worse mood compromises sleep. Although there is some empirical evidence indicating that sleep and mood have a bidirectional relationship (Lewis et al., 2023), evidence up to now has largely been mixed or stems primarily from aggregating findings across several studies (ten Brink et al., n.d.). Our longitudinal design with multiple testing points provides a unique opportunity to explore bidirectional links between sleep and mood within the same study and determine which drives changes in the other in adolescents with bipolar disorder. Two final secondary aims were to examine how sleep quality differed in adolescents with bipolar disorder relative to healthy controls and examine how sleep quality changed across treatment for bipolar disorder. We hypothesized that adolescents with bipolar disorder would have worse sleep quality than healthy controls, but it is unclear whether sleep quality would linearly improve across treatment since neither DBT nor SOC expressly focuses on sleep problems. Due to this, differences based on treatment group for the aims listed above can be found in the supplement. The effects of DBT vs. SOC on mood and suicide risk are covered in a separate report (Goldstein et al., 2024).

2. Materials & methods

2.1. Participants

Adolescents with bipolar disorder were recruited from a local clinic that specializes in diagnosing and treating youth with bipolar disorder. Inclusion criteria included: 12–18 years old with DSM-V (APA, 2013) criteria for Bipolar I, II, or validated research-operationalized criteria for Not Otherwise Specified (NOS, please see (Axelson et al., 2006; Hafeman et al., 2013)) diagnosed by semi-structured interview (K-SADS-PL: Schedule for Affective Disorders and Schizophrenia for School Aged Children: Lifetime version (Kaufman et al., 1997)) with an acute manic, depressive, or mixed episode within three months of study entry; currently engaged in a pharmacotherapy regimen or willing to proceed with a regimen; English language fluency; 3rd grade literacy level; able and willing to give informed consent/assent; and at least one family member willing to participate in skills training (if randomized to DBT).

Study exclusion criteria included evidence of intellectual disability, pervasive developmental disorder, or organic central nervous system disorder by the K-SADS-PL, parent report, medical history, or school records; a life-threatening medical condition requiring immediate treatment; and current victim of sexual or physical abuse. Participants also could not have a neurological or severe systemic medical illness or history of head trauma with loss of consciousness.

Healthy controls were recruited from an online university participant registry. Inclusion criteria for healthy controls included 12–19 years old, English language fluency, 3rd grade literacy level, and able and willing to give informed consent/assent. In addition to the exclusion criteria for adolescents with bipolar disorder, healthy controls were also excluded if they were taking non-psychiatric medications that affect the central nervous system or if they had a past history of a mood or anxiety disorder, current psychiatric diagnosis,

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first-degree relative with a history of bipolar disorder, or sibling enrolled in the current study. Controls additionally had to meet eligibility to participate in an fMRI scan associated with the larger study (data not included here; i.e., claustrophobia, body size greater than the MR bore, cardiac pacemakers, neural pacemakers, surgical clips in the brain or blood vessels, any metal in the body, and non-right handedness [scores <40 on the Edinburgh Handedness Inventory (Millar et al., 2004)]).

A total of 100 adolescents with bipolar disorder and 50 healthy controls were enrolled in the study. Of the adolescents with bipolar disorder, 25 were excluded from analyses for completing only the baseline visit and no subsequent visits (healthy controls only completed a baseline visit) or were enrolled prior to adding the PSQI to the assessment battery. This left a final sample size of 75 adolescents with bipolar disorder (DBT $n = 31$, SOC $n = 44$) and 50 healthy controls that were submitted to analyses. Demographic information for the final sample is in Table 1.

2.2. Procedure

2.2.1. Screening: All participants underwent a screening visit in which informed consent/assent was obtained and a diagnostic evaluation (K-SADS-PL) was conducted by trained evaluators. This diagnostic evaluation was administered first to the parent and then to the adolescent with scores based on a consensus between both. Adolescents with bipolar disorder additionally completed a clinical interview with a psychiatrist. Information from the diagnostic evaluation and clinical interview were used to confer on a diagnosis. Finally, a brief online screening questionnaire was completed on further details of their diagnosis, treatment, and current symptoms.

2.2.2. Treatment: Details regarding the study interventions can be found in Goldstein et al. (Goldstein et al., 2024). In brief, eligible adolescents with bipolar disorder were randomized to receive DBT or SOC. Treatment groups were balanced for sex assigned at birth, age, and history of suicide attempts (see Table 1). All participants, regardless of treatment assignment, received pharmacotherapy at the clinic by trained child psychiatrists. Pharmacotherapy was managed using flexible but standardized best practices based on guidelines established by the American Academy of Child and Adolescent Psychiatry for the management of pediatric bipolar disorder.

2.2.3. Assessment visits: Adolescents with bipolar disorder completed seven assessment visits (baseline, 3-months, 6-months, 9-months, 12-months, 18-months, 24-months). Healthy controls completed one baseline visit. During these visits, participants completed the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) to assess sleep quality, the Mood and Feelings Questionnaire (MFQ) (Angold et al., 1987; Costello and Angold, 1988) to assess depression severity, and adolescents with bipolar disorder also completed the ALIFE semi-structured interview (Keller et al., 1987) to obtain weekly Psychiatric Status Ratings (PSR).

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2.3. Materials

2.3.1. Pittsburgh Sleep Quality Index (PSQI): The PSQI assesses sleep quality over the past month (Buysse et al., 1989) and has adequate internal consistency and validity in adolescents (Raniti et al., 2018). Participants answer questions comprising 7 dimensions—sleep duration, sleep disturbance, sleep latency, daytime sleepiness, sleep efficiency, sleep quality, and sleep medications. Each dimension is scored between 0 and 3, with higher scores indicating greater dysfunction in that dimension; all sub scores are summed to produce a global score, between 0 and 21. A global PSQI score > 5 indicates poor sleep quality, with higher scores indicating worse sleep quality.

2.3.2. Mood and Feelings Questionnaire (MFQ): The MFQ (Angold et al., 1987; Costello and Angold, 1988) assesses depression symptoms in children and adolescents within the past two weeks. Adolescents indicated how much they agreed to 33 statements (ex: I hated myself, I thought my family would be better off without me). Higher scores indicate greater depression severity.

2.3.3. ALIFE Psychiatric Status Ratings (PSR): The ALIFE is a semi-structured interview (Keller et al., 1987) that yields Psychiatric Status Ratings (PSR) for depression, hypomania, suicidal ideation, and comorbid disorders for each week between the current visit and the previously attended visit. Ratings range from 0 to 2 (no to mild symptoms), 3 to 4 (subthreshold), and 5 to 6 (full threshold DSM-5 criteria). For the current analyses, we focus on depression, hypomania, and suicidal ideation PSR scores.

3. Statistical analyses

3.1. Baseline sleep quality

We performed a Chi-Square test to compare the number of participants with poor sleep quality (PSQI global score > 5) between adolescents with bipolar disorder and healthy controls. We performed independent *t*-tests to compare means on the PSQI between adolescents with bipolar disorder and healthy controls.

3.2. Longitudinal sleep quality changes

We performed a linear mixed effects model to account for the fact that not all participants completed a PSQI assessment at every visit. Visit (baseline, 3-month, 6-month, 9-month, 12-month, 18-month, 24-month), Treatment Group (DBT, SOC), and Visit X Treatment Group were entered as fixed effects. Subject was entered as a random effect (example syntax for this analysis can be found in Fig. S4 of the supplement). To understand the main effect of Visit, post-hoc Sidak-adjusted pairwise comparisons were performed. First, we compared each visit with the subsequent visit (e.g., baseline v. 3-month, 3-month v. 6-month, etc.) to assess the progression of sleep quality over time. We additionally compared each visit to the baseline visit to assess changes in sleep quality relative to study entry.

3.3. Predictive relationships between sleep quality and mood symptom ratings

We performed two separate sets of lag analyses (IBM SPSS Amos 28). The first set of analyses examined whether sleep quality (i.e., global PSQI score) predicted future mood

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symptom ratings for depression, hypomania, and suicidal ideation. The second set of lag analyses examined the inverse—whether mood symptom ratings predicted future sleep quality. Since the PSQI was collected once during each visit but symptom ratings were obtained weekly, the dates of each PSQI assessment were aligned to the closest PSR week for each participant, such that the number of days between the two was minimized. Surrounding weeks of PSR scores were then coded in reference to these aligned scores (+/− 1 week offset, +/− 2 weeks offset, etc).

For the set of lag models in which sleep quality predicted future mood symptoms, global PSQI score at each visit was directly entered into the model as a separate predictor and used to predict the next month's mood symptom severity (i.e., average of +1–4 weeks offset of PSR scores). Separate models were performed for depression, hypomania, and suicidal ideation symptoms.

Since depression is closely linked with suicidality, we performed an additional lag model for suicidal ideation with MFQ score at each visit predicting the next month of suicidal ideation, in addition to PSQI score, to control for depression severity. Since these analyses tested for relationships between sleep quality and mood symptoms, we removed the three statements about sleep and fatigue when calculating the MFQ total score (i.e., I didn't sleep as well as I usually sleep, I slept a lot more than usual, I felt too tired I just sat around and did nothing), resulting in scores between 0 and 60 (instead of 0–66).

We also performed lag models in which mood symptom scores predicted future sleep quality. Since the PSQI reflects sleep quality for the prior month (i.e., retrospective reporting), we used symptom ratings for the month before the PSQI *assessment timeframe* (i.e., average of −5-8 weeks offset of PSR scores), not the month before the PSQI *collection date* as the predictor. By doing so, we ensure that we examined predictive relationships, as intended, not cross-sectional relationships. Therefore, mood symptom scores the month before each PSQI assessment timeframe was directly entered into the model as a separate predictor and used to predict sleep quality at the subsequent upcoming visit.

For all lagged models, autoregressive effects were controlled for by incorporating terms in which each variable was predicted by the previous timepoint of that same variable (e.g., baseline PSQI predicts 3-month PSQI, 3-month PSQI predicts 6-month PSQI, etc). Error terms were included for all variables which were being predicted by another variable. See Fig. 1 for an example of the lagged model structure.

3.4. Relationships between sleep quality and suicide attempts

Given the small sample size for suicide attempts and that suicide attempts did not always occur in the month following a PSQI assessment, we were unable to run the same lag analysis that we performed on the other PSR scores. Nonetheless, because suicide attempts are a clinically important measure, we ran exploratory analyses to examine any potentially meaningful relationships between sleep quality and suicide attempts. We performed an independent *t*-test to examine differences in average sleep quality across all visits for adolescents who had a suicide attempt compared to adolescents who had no suicide attempts. We performed a paired samples t-test to examine whether sleep quality differed

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in the month prior to a suicide attempt during the study timeframe compared to a month without a suicide attempt. Similar to the analyses with suicidal ideation, we conducted both *t*-tests with and without MFQ score as a covariate to control for depression severity.

4. Results

4.1. Baseline sleep quality

The PSQI was added to the study 11 months into enrollment. Thus, 58 of the 75 adolescents with bipolar disorder had a baseline PSQI score. Since healthy controls were added to the study later, all 50 had a baseline PSQI score. The majority of adolescents with bipolar disorder (75.9 %, $n = 44/58$) had a PSQI score >5, reflecting poor sleep quality—significantly larger than the 18 % ($n = 9/50$) of healthy controls, $\chi^2(1, N = 108) = 35.97$, $p < .001$. Overall, the average global PSQI score at baseline for adolescents with bipolar disorder ($M = 8.86$, SD = 4.30) was significantly higher (i.e., worse) than healthy controls ($M = 3.56$, SD = 4.30). Adolescents with bipolar disorder also reported significantly higher scores in all seven dimensions of the PSQI compared to healthy controls. See Table 2 for means, *t*-test statistics, and effect sizes. Overall, the effect sizes for these differences were medium to large, with the largest effect sizes for the global score ($d = 1.52$), daytime sleepiness ($d = 1.43$), and sleep medications ($d = 1.24$). Given that the global PSQI score combines dysfunction across all dimensions and showed the most robust difference between groups, we focus on the global score for the remaining analyses.

4.2. Longitudinal sleep quality changes

Using a linear mixed effects model, we examined how sleep quality changed over time, across treatment and post-treatment follow-up, in adolescents with bipolar disorder. There was a significant main effect of Visit, $F(6, 223.77) = 4.98$, $p < .001$, which we followed up with post-hoc pairwise comparisons to better understand the progression of sleep quality over time. Global PSQI score decreased (i.e., improved) between the baseline and the 3-month visits, $M_{diff} = -2.01$, SE = 0.55, $p = .006$, and then remained stable thereafter between subsequent visits, $ps > .478$. See Fig. 2 and Fig. S1 in the supplement for sleep quality separated by treatment group. Global PSQI score was lower (i.e., improved) at every visit relative to baseline sleep quality, $ps < .042$, except for the 12-month visit which was similar to baseline sleep quality, $M_{diff} = -1.40$, SE = 0.55, $p = .207$. Statistics for effects involving Treatment Group are in the supplement, but these were not significant.

At the 12-month visit (i.e., end of treatment), 61.5 % ($n = 32/52$) of adolescents with bipolar disorder had a global PSQI score > 5, meeting the criteria for poor sleep quality, which was over 14 % fewer than at baseline. At the 24-month visit, 71.4 % ($n = 40/56$) of adolescents with bipolar disorder had a global PSQI score > 5, which was approximately 4.5 % fewer than at baseline.

4.3. Predictive relationships between sleep quality and mood symptom ratings

4.3.1. Sleep quality predicts future mood symptoms: Sleep quality at the 6-month visit significantly predicted the next month of depression, hypomania, and suicidal ideation scores. Sleep quality at the 9-month and 18-month visits both marginally predicted the

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subsequent month of depression and suicidal ideation scores. All of these relationships indicated that worse sleep quality predicted worse mood symptom ratings the following month. Sleep quality at the baseline, 3-month, and 12-month visits did not predict the next month of mood symptom scores. See Fig. 3 for a depiction of how sleep quality predicted future mood symptoms over time, Fig. S2 in the supplement for a depiction separated by treatment group, and the supplemental results for analyses on PSQI dimension scores predicting future mood symptoms. The unstandardized beta coefficients indicated that every 1-point increase on the PSQI resulted in a ~ 0.04–0.12 increase in mood scores, which is roughly equivalent to a 0.7–2 % worsening of symptoms. Comparing standardized coefficients between models (see Table 3 and Tables S1 & S2 in the supplement for effects by treatment group), shows that sleep quality appeared to have roughly an equivalent effect on depression, suicidal ideation, and hypomania (0.24–0.32). Relationships between sleep quality and suicidal ideation did not survive when controlling for depression severity. However, sleep quality was significantly correlated with depression severity, such that those with worse sleep quality also had worse depression severity at each visit (rs > 0.367, *ps* < .006).

4.3.2. Mood symptoms predict sleep quality:

Depression and suicidal ideation symptom severity both predicted future sleep quality at the baseline and 18-month visits. Depression symptoms also significantly predicted future sleep quality at the 3-month visit and suicidal ideation symptoms also significantly predicted future sleep quality at the 12-month visit. All of these relationships indicated that worse symptom ratings predicted worse future sleep quality. Mood symptoms at the 6-month, 9-month, and 24-month visits did not predict future sleep quality. See Fig. 4 and Fig. S3 in the supplement for effects separated by treatment group.

4.4. Relationships between sleep quality and suicide attempts

Over a third of adolescents with bipolar disorder had at least one suicide attempt during the two-year study duration (37 %; range = 0–65 attempts; $M = 6.25$, $SD = 15.83$ attempts among adolescents with a suicide attempt). Adolescents who had any suicide attempts had worse average sleep quality across all visits ($M = 8.15$, $SD = 3.02$) compared to adolescents with no suicide attempts ($M = 6.49$, $SD = 2.81$), $t(73) = 2.41$, $p = .019$, $d = 0.57$. This effect dropped to marginally significant when controlling for depression severity, $p = .059$. Sleep quality was on average worse preceding months with a suicide attempt ($M = 10.56$, $SD = 3.22$) compared to months with no suicide attempts ($M = 8.54$, $SD = 3.29$), $t(5) = 2.65$, $p = .045$, $d = 1.08$. This analysis should be interpreted with caution since only 6 adolescents met the criteria for having instances of both suicide attempts and no suicide attempts in the month following a PSQI assessment. Nonetheless, none of these six individuals had worse sleep quality preceding a month with no attempts compared to a month with attempts. This effect did not survive when controlling for average depression severity, $p = .369$. However, average sleep quality was significantly correlated with average depression severity, $r = 0.539$, $p < .001$. We do not test for treatment group effects for the above analyses in the supplement given the small sample size.

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4.5. Summary of results

Adolescents diagnosed with bipolar disorder had poor sleep quality at baseline relative to healthy controls. Sleep quality improved early in treatment among the youth with bipolar disorder, regardless of treatment assignment, but did not continue to improve linearly across treatment. Furthermore, the majority of adolescents still had PSQI scores above the criterion score of 5, indicating poor sleep quality. Sleep quality tended to predict the next month of mood symptoms in the middle of treatment, whereas mood symptoms tended to predict future sleep quality early in treatment, at the end of treatment, or during the post-treatment follow-up. Sleep quality was worse for adolescents who had a suicide attempt compared to those who did not have an attempt, and notably, sleep quality was worse preceding months with a suicide attempt compared to months with no attempts. Effects of sleep quality on suicidal ideation and suicide attempts did not survive when controlling for depression severity, although, sleep quality and depression severity are correlated.

5. Discussion

We examined relationships between sleep quality and mood symptoms in adolescents with bipolar disorder across a two-year longitudinal randomized controlled trial. The primary aim was to determine whether sleep quality predicted future mood symptoms, with secondary aims to examine the inverse (i.e., if mood symptoms predicted future sleep quality) and determine how sleep quality compared to healthy controls and how sleep quality changed across treatment for bipolar disorder. Results showed that adolescents with bipolar disorder commonly experience poor sleep quality which persisted across treatment, despite an initial improvement. Poor sleep quality and worse mood symptoms predicted subsequent worsening in the other, although at different times. Finally, poor sleep quality was also related to more suicide attempts, providing additional evidence that targeting sleep problems may be worthwhile in this population—both for improving sleep itself and for the potential benefits for mood and suicide risk.

Sleep quality, measured using the Pittsburgh Sleep Quality Index, was poor in adolescents with bipolar disorder. Replicating others (Cretu et al., 2016), sleep quality was worse than healthy controls, with a large effect size (Cohens d = 1.52). Whereas sleep quality improved early in treatment (between the baseline and 3-month visit), it did not continue to improve linearly over the course of treatment. Targeting sleep was not a core tenet in either treatment for bipolar disorder examined (DBT or SOC). Therefore, sleep quality may have exhibited an initial improvement by virtue of treating mood symptoms (mood symptoms did predict sleep quality early in treatment). However, there may be a limit to how much sleep quality will improve without explicit sleep intervention (Nierenberg et al., 1999). Indeed, sleep quality still tended to be poor (i. e., PSQI > 5) even after the initial improvement. These findings are in line with what others have found that sleep remains poor even in euthymic individuals with bipolar disorder (Cretu et al., 2016; Millar et al., 2004; Harvey et al., 2005). Thus, poor sleep quality may not simply be a symptom of bipolar disorder that is alleviated by treating the mood symptoms of the disorder.

Corroborating findings that sleep quality may precede changes in mood symptoms or the onset of bipolar disorder (Ritter et al., 2015; Shaw et al., 2005; Egeland et al., 2000; Lish et

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al., 1994; Duffy et al., 2010; Sierra et al., 2007; Bauer et al., 2006; Cretu et al., 2016), sleep quality at the 6-month visit significantly predicted the next month of depression, hypomania, and suicidal ideation. Adolescents in the current study were already diagnosed with bipolar disorder, so we do not know whether poor sleep quality may have preceded and contributed to the onset of the disorder itself, however, these findings suggest that better sleep quality may be a protective factor against the worsening of mood symptoms within the trajectory of the disorder. Furthermore, sleep quality was also related to suicide attempts, such that adolescents with a suicide attempt during the study had worse average sleep quality relative to adolescents who had no suicide attempts. In addition, in a small subset of participants, sleep quality was worse preceding months with a suicide attempt compared to months with no suicide attempts. Thus, across different analyses, we find support that sleep quality is linked to suicidality—both ideation and attempts. These findings add to the growing body of literature indicating the importance of sleep in mood episode recurrence within individuals with bipolar disorder (Ritter et al., 2015; Shaw et al., 2005; Egeland et al., 2000; Lish et al., 1994; Duffy et al., 2010; Sierra et al., 2007; Bauer et al., 2006; Cretu et al., 2016) and are also in line with other predictive models in healthy samples indicating that sleep is a predictor of mood changes (Bouwmans et al., 2017; Finan et al., 2015). In light of these findings, detailed prospective tracking of sleep quality may help identify adolescents at highest risk for suicide attempts as well as periods of elevated risk for attempt. Moreover, incorporating evidence-based sleep intervention within or alongside existing treatments for bipolar disorder may hold promise to prevent or stave off recurrence of mood symptoms and suicidality. Indeed, there is some evidence that treating insomnia symptoms in adults with bipolar disorder improves sleep and reduces risk of relapse of any mood episode (Harvey et al., 2015).

While sleep quality predicted mood symptoms, we also found the inverse—mood symptoms predicted future sleep quality. Specifically, depression predicted future sleep quality at the baseline, 3-month, and 18-month visits. Suicidal ideation predicted future sleep quality at the baseline, 12-month, and 18-month visits. Hypomania was never predictive of future sleep quality. Hypomania symptom severity in our sample tended to be low and, whereas, sleep problems are one of the most common precipitants for hypomania in individuals with bipolar disorder (Morton and Murray, 2020) and treating sleep problems may be particularly effective for reducing hypomania relapse (Harvey et al., 2015), the reverse relationship of hypomania predicting sleep quality may be weaker. Broadly, our findings support the longstanding notion that sleep and mood have a bidirectional relationship (Lewis et al., 2023; Harvey, 2008). A recent longitudinal study in adults with bipolar disorder indicated strong bidirectional relationships between sleep and depressive symptoms but weaker bidirectional relationships between sleep and hypomania symptoms (Lewis et al., 2023). Our findings in adolescents with bipolar disorder broadly corroborate these findings, although the weaker sleep-hypomania bidirectional relationship in our sample appeared to be driven by hypomania being a poor predictor of sleep, rather than the reverse (Lewis et al., 2023). Importantly, the bidirectional hypomania-sleep relationship may depend on individual differences including age, sex assigned at birth, and bipolar diagnosis (Bauer et al., 2006; Lewis et al., 2023), which may explain this difference in our adolescent sample. It is also worth noting that it was never the case across the entire sample that both sleep

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and mood symptoms predicted the other at the same timepoint. Potentially, time in treatment may be an important consideration, such that sleep quality only becomes predictive of mood symptoms in the middle of treatment, after mood symptoms have started to improve. Alternatively, the bidirectional relationship between sleep and mood may be cyclical rather than simultaneous. In other words, an improvement in mood symptoms (due to treatment or other factors) leads to an improvement in sleep quality, which in turn further improves mood symptoms, and so on. Indeed, although a single night of poor sleep may worsen mood symptoms the following day, it is more likely that several nights or weeks of poor sleep need to accumulate to result in consistent worsening of symptoms. This may be why we see roughly an alternating trend in the current study with mood predicting sleep early in treatment, sleep predicting mood mid-treatment, and then mood predicting sleep again at the end of treatment/post-treatment follow-up. Furthermore, mood symptoms may predict sleep quality more consistently (βs: 0.23, 0.24, 0.25, 0.28, 0.32, 0.33), given the number of significant relationships, but the estimates for sleep quality predicting mood symptoms appeared to be slightly larger (βs: 0.29, 0.30, 0.32), although the strength of these relationships between models seemed fairly comparable.

Although sleep quality predicted future suicidal ideation and was related to suicide attempts, these relationships did not persist when controlling for depression severity. Depression and suicidality are tightly linked so, on one hand, it may not be surprising that controlling for depression severity weakened the link between sleep quality and suicidality. Nonetheless, sleep quality at the 6-month visit also predicted the next month of depression symptoms (in addition to the next month of suicidal ideation). One consideration may be that poor sleep quality increases depression severity and depression severity, in turn, worsens suicidality. We also note that sleep quality and depression severity were significantly correlated with each other. This was the case even when the sleep and fatigue statements on the MFQ were removed from scoring. Thus, there appears to be some amount of overlap in what each assessment (PSQI and MFQ) is measuring and, by controlling for depression severity, we may also be controlling for an important aspect that the PSQI is also tapping into. Given the clinical importance and real-life impact of suicidal ideation and suicide attempts, it is potentially fruitful to consider sleep quality as an important treatment target in adolescents with bipolar disorder.

There are a few limitations of this study that are important to acknowledge. First, the weekly PSR assessments for depression, hypomania, and suicidal ideation symptoms were reported retrospectively (symptoms were rated at each assessment visit by a clinician for each week between the current visit and the prior visit). Second, while the PSQI is a widely used measure of sleep quality, there may be other aspects of sleep that are related to mood symptoms that are not necessarily captured in the PSQI. For example, slow-wave sleep and REM sleep have been implicated in emotion regulation (Walker, 2009; Van Der Helm et al., 2011; Gujar et al., 2011; Rosales-Lagarde et al., 2012; Ochsner and Gross, 2005) and are often altered in psychiatric conditions, including bipolar disorder (Zangani et al., 2020). Relatedly, examining other measures of sleep, both objective (e.g., sleep architecture via polysomnography or with actigraphy) and subjective, could help to identify more targeted treatments for sleep that would balance impact with patient burden. We also cannot determine whether the improvement in sleep quality between the baseline and 3-month visit

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was due to the treatment protocol or other factors, such as habituation to the study visits or changes over time unrelated to treatment. Lastly, there may have been differences between our sample and the broader population of adolescents with bipolar disorder that could have influenced sleep quality and mood relationships. For example, suicide attempts were high in our sample (Serra et al., 2022), which may have been due to a higher referral rate for high-risk adolescents given that DBT is known to be effective for treating suicide risk. However, our sample also shared several similarities to previously published work including comorbid conditions (Frías et al., 2015; Fahrendorff et al., 2023) (reported in Goldstein et al. (Goldstein et al., 2024)), number of prescribed medications which tends to be high in youth with bipolar disorder (Vande Voort et al., 2016), and predominantly female for a treatment seeking sample.

6. Conclusion

Adolescents with bipolar disorder may benefit from evidence-based sleep interventions in addition to existing treatment approaches for bipolar disorder. Poor sleep quality is, at a minimum, a common symptom of adolescent bipolar disorder that does not appear to improve fully with treatment of mood symptoms alone. More importantly, poor sleep quality may play a role in the worsening of mood symptoms and suicidality. Thus, treating sleep may be another pathway with which to improve mood symptoms, reduce deaths by suicide, and improve quality of life in this at-risk population. The best treatment approach may be to treat both sleep and mood symptoms as early as possible and simultaneously as waiting to treat either could hinder progress in treating the other, which would be important to explore in future treatment studies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability

The data that support the findings of this study are available on request from the corresponding author.

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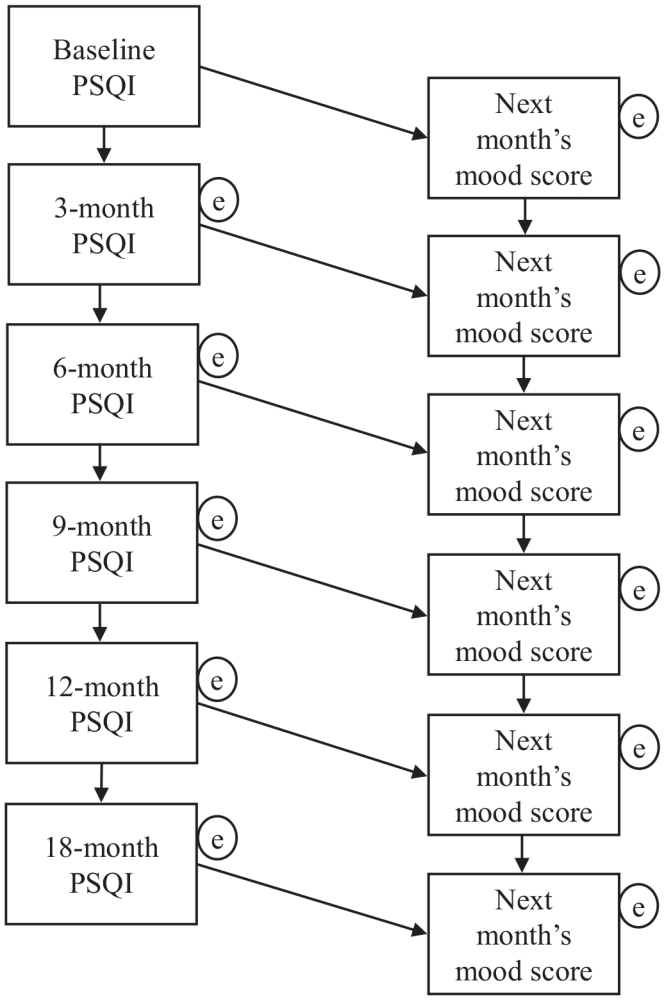

Fig. 1.

Example of lagged model structure. Diagonal arrows represent lagged relationships in which each predictor (boxes to the left; e.g., Pittsburgh Sleep Quality Index [PSQI]) is a separate variable entered in the model used to predict future scores of a particular outcome (boxes to the right; e.g., the next month's average mood [depression, suicidal ideation, hypomania] score). Downward arrows between predictors and outcomes control for autoregressive effects. Circles with e represent error terms.

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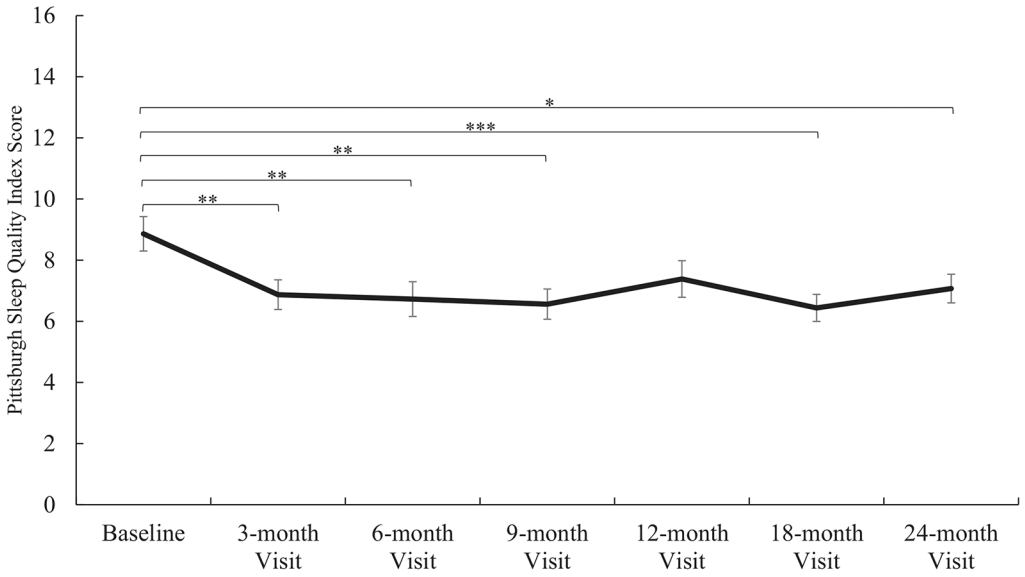

Fig. 2.

Changes in sleep quality across treatment (baseline – 12-month visits) and post-treatment follow-up (18- and 24-month visits), with higher scores representing worse sleep quality. Sleep quality is collapsed across treatment group (Dialectical Behavioral Therapy vs Standard of Care), since scores did not differ by treatment group. Error bars represent standard error. *$p < .05$, **$p < .01$, ***$p < .001$.

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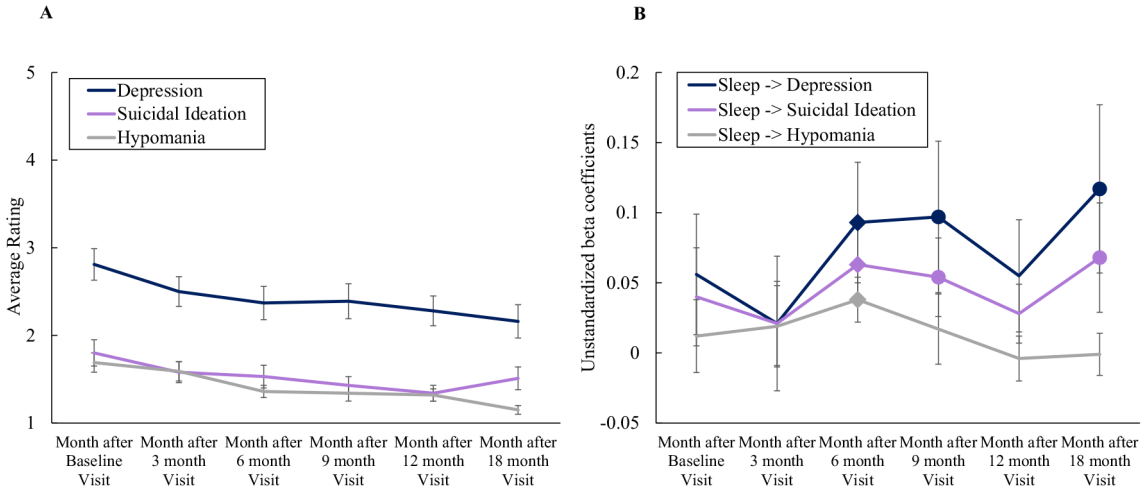

Fig. 3.

A: Changes in average depression, suicidal ideation, and hypomania symptom ratings the month after each assessment visit. B: Unstandardized beta coefficients for sleep quality (i.e., Pittsburgh Sleep Quality Index global score) predicting the following month of mood symptom ratings. Diamond symbol represents timepoints in which sleep quality significantly ($p < .05$) predicted mood symptoms. Circle symbol represents timepoints in which sleep quality marginally ($p < .10$) predicted mood symptom ratings. Error bars represent standard error.

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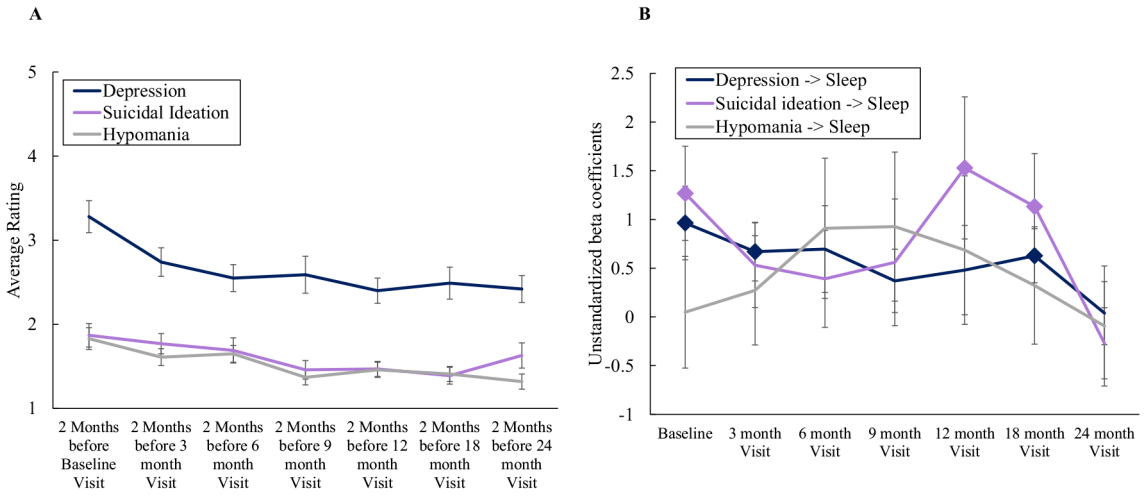

Fig. 4.

A: Changes in average depression, suicidal ideation, and hypomania symptom ratings for the month timeframe two months before each assessment visit. B: Unstandardized beta coefficients for Psychiatric Status Ratings predicting future sleep quality (i.e., Pittsburgh Sleep Quality global score). Diamond symbol represents timepoints in which mood symptoms significantly ($p < .05$) predicted sleep quality. Error bars represent standard error.

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Table 1

Sociodemographic and Clinical Information.

	Dialectical Behavior Therapy	Standard of Care	Healthy Controls
n	31	44	50
Age at Consent	*M* = 15.82 (*SD* = 1.87)	*M* = 16.19 (*SD* = 1.46)	*M* = 16.13 (*SD* = 2.41)
Age of Bipolar Disorder Onset	*M* = 12.91 (*SD* = 3.52)	*M* = 14.04 (*SD* = 2.27)	–
Lifetime Suicide Attempts	2.71 (*SD* = 5.45)	2.00 (*SD* = 4.27)	–
N of Psychotropic Medications	*M* = 2.35 (*SD* = 1.47)	*M* = 2.25 (*SD* = 1.30)	–
Sex Assigned at Birth			
Female	26	39	40
Male	5	5	9
Race			
White	22	36	30
Black	5	5	8
Asian	0	1	5
Multiracial	2	2	6
Undisclosed	2	0	0
Ethnicity			
Not Hispanic	29	40	46
Hispanic	2	4	3
Subtype			
Bipolar I	4	8	–
Bipolar II	7	9	–
Bipolar NOS	20	27	–

Note. One person from the healthy control group was missing demographic information.

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Table 2

Baseline Pittsburgh Sleep Quality Index Scores.

	Adolescents w/Bipolar Disorder *n* = 58	Healthy Controls *n* = 50	*t*	*p*	Cohen's *d*
Sleep duration	0.84 (1.09)	0.20 (0.57)	3.76	< .001	0.73
Sleep disturbance	1.33 (0.69)	0.74 (0.44)	5.20	< .001	1.00
Sleep latency	1.62 (1.14)	0.96 (0.92)	3.28	.001	0.63
Daytime sleepiness	1.41 (0.94)	0.30 (0.54)	7.39	< .001	1.43
Sleep efficiency	0.76 (1.11)	0.34 (0.63)	2.36	.020	0.45
Sleep quality	1.52 (0.82)	0.90 (0.82)	4.71	< .001	0.90
Sleep medications	1.38 (1.35)	0.12 (0.33)	6.44	< .001	1.24
Global score	8.86 (4.30)	3.56 (4.30)	7.86	< .001	1.52

Note: Higher scores indicate greater dysfunction. Scores range from 0 to 3 for the seven categories and range from 0 to 21 for the global score. Standard deviation in parentheses.

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Table 3

Statistics from lagged models.

	Depression	Hypomania	Suicidal Ideation	Suicidal Ideation (controlling for depression)
Sleep Quality Predicts the Next Month's Mood Symptoms				
Baseline PSQI → mood scores	B = 0.056, SE = 0.043, p = .193, β = 0.169	B = 0.012, SE = 0.026, p = .631, β = 0.063	B = 0.040, SE = 0.035, p = .249, β = 0.150	B = −0.028, SE = 0.030, p = .343, β = −0.103
3-month PSQI → mood scores	B = 0.021, SE = 0.048, p = .662, β = 0.062	B = 0.019, SE = 0.029, p = .509, β = 0.093	B = 0.021, SE = 0.030, p = .472, β = 0.085	B = 0.014, SE = 0.029, p = .635, β = 0.055
6-month PSQI → mood scores	**B = 0.093,SE = 0.043, p = .031, β =0.297**	**B = 0.038, SE= 0.016, p = .020, β =0.319**	**B = 0.063,SE = 0.029, p = .032, β= 0.291**	B = 0.037, SE = 0.028, p = .184, β = 0.179
9-month PSQI → mood scores	B = 0.097, SE = 0.054, p = .073, β = 0.240	B = 0.017, SE = 0.025, p = .503, β = 0.104	B = 0.054, SE = 0.028, p = .057, β = 0.278	B = 0.015, SE = 0.026, p = .578, β = 0.080
12-month PSQI → mood scores	B = 0.055, SE = 0.040, p = .168, β = 0.185	B = −0.004, SE = 0.016, p = .798, β = −0.036	B = 0.028, SE = 0.021, p = .180, β = 0.182	B = 0.025, SE = 0.020, p = .226, β = 0.164
18-month PSQI → mood scores	B = 0.117, SE = 0.060, p = .052, β = 0.278	B = −0.001, SE = 0.015, p = .931, β = −0.013	B = 0.068, SE = 0.039, p = .086, β = 0.249	B = 0.029, SE = 0.038, p = .444, β = 0.108
Mood Symptoms Predict Future Sleep Quality				
Mood → baseline PSQI	**B = 0.964,SE = 0.378, p= .011, β =0.319**	B = 0.048, SE = 0.573, p = .933, β = 0.011	**B = 1.268,SE = 0.484,p = .009, β= 0.326**	–
Mood → 3-month PSQI	**B = 0.670,SE = 0.301, p = .026, β = 0.232** B = 0.696, SE	B = 0.273, SE = 0.561, p = .626, β = 0.054 B = 0.910, SE	B = 0.531, SE = 0.434, p = .221, β = 0.133 B = 0.391,	–
Mood → 6-month PSQI	= 0.445, p = .118, β = 0.203 B = 0.370, SE	= 0.719, p = .205, β = 0.165 B = 0.927, SE	SE = 0.498, p = .432, β = 0.104 B = 0.560,	–
Mood → 9-month PSQI	= 0.325, p = .255, β = 0.161	= 0.765, p = .226, β = 0.171	SE = 0.650, p = .389, β = 0.122	–
Mood → 12-month PSQI	B = 0.481, SE = 0.459, p = .295, β = 0.126	B = 0.686, SE = 0.762, p = .368, β = 0.109	**B = 1.529,SE = 0.729,p = .036, β= 0.244**	–
Mood → 18-month PSQI	**B = 0.628,SE = 0.278, p= .024, β =0.276**	B = 0.323, SE = 0.602, p = .591, β = 0.067	**B = 1.133,SE = 0.544,p = .037, β= 0.255**	–
Mood → 24-month PSQI	B = 0.039, SE = 0.323, p = .903, β = 0.014	B = −0.093, SE = 0.616, p = .880, β = −0.017	B = −0.270, SE = 0.365, p = .459, β = −0.084	–

Note: PSQI = Pittsburgh Sleep Quality Index. B = unstandardized beta coefficient, β = standardized beta coefficient, SE = standard error. Significant effects are bolded.