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Outcomes of the Transdiagnostic Intervention for Sleep and Circadian Dysfunction (TranS-C) in a community setting: Unpacking comorbidity

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Abstract

Objective: Comorbidity and subdiagnostic symptoms are understudied for sleep and circadian problems. We evaluated 1) impairment associated with (a) number of sleep and circadian problems and (b) diagnostic threshold (full diagnosis vs. subdiagnostic symptoms), and 2) Transdiagnostic Sleep and Circadian Intervention (TranS-C) outcomes for participants with specific sleep and circadian problems.

Method: Community participants (N=121) with serious mental illness and sleep and circadian problem(s) were randomized to receive TranS-C plus usual care (TranS-C+UC) or usual care plus delayed TranS-C (UC-DT). Overall impairment, psychiatric symptoms, and sleep and circadian dysfunction were assessed at pre-treatment, post-treatment, and 6-month follow-up.

Results: Higher numbers of sleep and circadian problems, versus one problem, were associated with worse overall impairment, psychiatric symptoms, and sleep and circadian dysfunction (ps<0.05, ω^2=0.06–0.15). Diagnostic threshold was not associated with baseline functioning (ps>0.05). TranS-C+UC versus UC-DT was associated with psychosocial and sleep and circadian improvements for specific sleep and circadian problems (insomnia, hypersomnia, parasomnias, periodic limb movement/restless leg syndrome, circadian rhythm disorders), though improvements varied by problem. TranS-C+UC outcomes were not moderated by number of sleep and circadian problems (ps>0.05).

Conclusion: Higher numbers of sleep and circadian problems, not diagnostic threshold, were associated with greater impairment. Transdiagnostic utility of TranS-C+UC was supported.

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Keywords

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Introduction[1]

Comorbidity among mental illness is pervasive. More than 40% of 12-month mental illness cases in the U.S. are estimated to be comorbid, and in turn, comorbidity is associated with greater clinical severity and poorer functioning (Kessler et al., 2005). However, when developing treatments for mental illness, randomized controlled trials often exclude patients with comorbid diagnoses. Similarly, trials regularly overlook comorbid subdiagnostic symptoms, defined as core symptoms of a disorder in the absence of meeting full diagnostic criteria (Wolitzky-Taylor et al., 2014). These practices persist despite calls for dimensional approaches to mental illness (Cuthbert & Insel, 2013) and evidence that subdiagnostic symptoms are common and associated with psychosocial impairment (e.g., Balazs et al., 2013; Marangell, 2004). Promisingly though, comorbid disorders and select subdiagnostic symptoms can be effectively targeted via psychosocial treatments (Cuijpers et al., 2007; McHugh et al., 2009).

Transdiagnostic treatments, or treatments that concurrently target cognitive and behavioral processes common to different mental illness, hold promise for treating comorbid diagnoses and subdiagnostic symptoms. The transdiagnostic approach to mental illness proposes that disorders co-occur, at least in part, because they share common processes that causally contribute to the development or maintenance of symptoms (Dalgleish et al., 2020; Mansell et al., 2009). Thus, targeting these common processes may represent an efficient path for treatment (Harvey et al., 2004).

Using data from a randomized controlled trial (NCT02469233; Harvey et al., 2021), the present study focused on a transdiagnostic treatment for sleep and circadian problems—the Transdiagnostic Sleep and Circadian Intervention (TranS-C)—delivered to individuals diagnosed with a serious mental illness (SMI). Sleep and circadian problems have been proposed as a transdiagnostic mechanism of SMI (Harvey et al., 2011). Evidence to support this proposal includes that a) sleep and circadian problems—such as insomnia, hypersomnia, and evening circadian preference—predict and predate psychiatric symptoms, including depression, substance use, anxiety, and psychosis (Hertenstein et al., 2019; Kaplan et al., 2015; Kivela et al., 2018), b) common cognitive, behavioral, and biological processes maintain sleep and circadian problems as well as SMI (Harvey, 2004), and c) interventions targeting sleep and circadian problems are associated with improved psychiatric symptoms (Taylor & Pruiksma, 2014). Indeed, TranS-C, which is grounded in the Sleep Health Framework (Buysse, 2014), is associated with reductions in sleep-related problems, functional impairment, and psychiatric symptoms.

[1]Abbreviations: ANCOVA = analysis of covariance; SMI = serious mental illness; TranS-C = Transdiagnostic Intervention for Sleep and Circadian Disorders; UC = Usual Care; UC+DT = usual care followed by delayed treatment; 6FU = 6-month follow-up.

However, there are gaps in this prior research exploring comorbidity, subdiagnostic symptoms, and TranS-C outcomes. First, although there is a relatively robust literature on sleep and circadian problems that are comorbid with mental (e.g., Ford et al., 1989) or physical (e.g., Parish et al., 2009) illness, past research on comorbidities *between* sleep and circadian problems is limited. This small body of research has primarily focused on testing a single sleep and circadian comorbidity (e.g., insomnia and hypersomnia in a major depressive episode; Geoffroy et al., 2018), outcomes collapsing across sleep and circadian comorbidities (e.g., Harvey et al., 2021; Reeve et al., 2019), or comorbidities between common sleep symptoms assessed in isolation (e.g., Roth et al., 2006). Second, this research on sleep and circadian problems has not yet extended to subdiagnostic symptoms. Together, impairment associated with a) different numbers of sleep and circadian problems and b) levels of diagnostic threshold (e.g., full diagnosis versus subdiagnostic symptoms) of sleep and circadian problems is unknown. Elucidating these relationships is critical for clarifying the functional impact of sleep and circadian problems. Third, prior evaluation of TranS-C has collapsed across all patients, who presented with a range of comorbid sleep and circadian problems (Harvey et al., 2021). Thus, the efficacy of TranS-C for *specific* sleep and circadian problems and varying *numbers* of sleep and circadian problems has not yet been tested. This represents an important next step to help clinicians determine whether TranS-C could be an appropriate choice for a given patient's sleep and circadian problems.

The present study sought to address these gaps in the literature. Aim 1 sought to test the relationships between 1a) *number* of sleep and circadian problems and baseline functioning, and 1b) *diagnostic threshold* of sleep and circadian problems and baseline functioning. For Aim 1a, we coded each participants' number of sleep and circadian problems. For Aim 1b, we coded whether each participants' sleep and circadian problems met diagnostic threshold, categorized as follows: full diagnoses only, full diagnoses plus other subdiagnostic symptoms, and subdiagnostic symptoms only. Hypothesis 1a was that, controlling for diagnostic threshold of sleep and circadian problems, *higher numbers* of sleep and circadian problems would be associated with poorer baseline functioning – specifically, more severe functional impairment, psychiatric symptoms, and sleep and circadian dysfunction (i.e., sleep disturbance, sleep-related daytime impairment, and sleep health). Hypothesis 1b was that, controlling for number of sleep and circadian problems, *diagnostic threshold* would be associated with poorer baseline functioning, such that full diagnoses would be associated with the poorest functioning, followed by full diagnoses plus other subdiagnostic symptoms, then subdiagnostic symptoms only. The latter hypothesis was based on a key premise of widely-used categorical approaches to diagnosis in research, policy, and clinical practice – namely that diagnostic threshold signifies the presence of clinically and functionally meaningful symptoms (e.g., Clark et al., 2017). To summarize, with Aim 1, we sought to disentangle the functional impact of diagnostic threshold from number of sleep and circadian problems, and thereby isolate the distinct relationships between impairment and 1a) number of sleep and circadian problems, and 1b) diagnostic threshold of sleep and circadian problems.

Aim 2 sought to evaluate the effects of TranS-C plus Usual Care (TranS-C+UC) versus Usual Care followed by Delayed Treatment with TranS-C (UC-DT) for individuals with specific sleep and circadian problems and varying numbers of sleep and circadian problems.

Hypothesis 2 was that TranS-C+UC would be associated with better outcomes than UC-DT at post-treatment and 6-month follow-up on outcomes of functional impairment, general psychiatric symptoms, and sleep and circadian dysfunction for all specific sleep and circadian problems. We also hypothesized that TranS-C+UC would not be moderated by number of sleep and circadian problems.

Method

Participants and Procedures

Data from participants (N=121) in this study were collected during a randomized controlled trial funded by the National Institute of Mental Health (Harvey et al., 2016; Harvey et al., 2021; NCT02469233). Participants who met criteria for SMI were recruited from multiple sites within Alameda County Behavioral Health Care Services (ACBHCS), a community mental health center in California. SMI was operationalized according to Public Law 102–321 and previous research (Wang et al., 2002) as the presence, for 12 months, of at least one Diagnostic and Statistical Manual–5 (DSM-5; American Psychiatric Association, 2013) mental disorder leading to substantial interference with one or more major life activities.

To enhance representativeness and generalizability, inclusion and exclusion criteria were kept to a minimum. Inclusion criteria included: 1) Age 18+ years; 2) English language fluency; 3) presence of at least one DSM-5 mental disorder for 12 months; 4) having a guaranteed bed to sleep in for 3 months; 5) receiving care for SMI at ACBHCS; 6) consenting to regular communications between research team and psychiatrist and/or case manager; and 7) experiencing one or more sleep or circadian problems for at least 3 months assessed with the Sleep and Circadian Problems Interview, which is an adapted version of the Insomnia Interview Schedule (Morin, 1993).

The exclusion criteria included: 1) presence of an active and progressive physical illness or neurological degenerative disease and/or substance abuse/dependence making participation in the study infeasible; 2) current serious suicide or homicide risk (assessed by research staff, a case manager, or psychiatrist); 3) night shift work >2 nights per week in the past 3 months; 4) pregnancy or breast-feeding; 5) not able/willing to complete the pre-treatment assessments. Individuals with periodic limb movement disorder often have comorbid insomnia, poor sleep habits, and can benefit from CBT-I (Edinger et al., 1996). Hence, these individuals were included in this study. As participants' SMI medications often need to be changed, excluding on this basis is neither feasible nor representative of clinical practice. Medication use and changes were recorded.

Participants were randomly allocated to TranS-C+UC (n=61) or 6-months of UC-DT (n=60). Randomization was stratified by age (0=under 50 years, 1=50+ years) and psychosis (0=no, 1=yes). Participants completed assessments at pre-treatment, immediately post-treatment (9–14 weeks later), and 6-month follow-up (6FU). Assessors were blind to treatment allocation. The University of California, Berkeley Committee for the Protection of Human Subjects approved the study, and informed consent was obtained from all participants. See Supplement for CONSORT diagram (Figure 1, supplement). A full description of study procedures is detailed in Harvey et al. (2021).

Treatment Conditions

TranS-C+UC—TranS-C is driven by case conceptualization. It includes four cross-cutting interventions in every session, four core modules that apply to most participants, and seven optional modules applied based on patient presentation. The average number of 50-minute sessions attended was eight. Up to 12 sessions could be provided but was rarely needed. See Table 1 for summary of treatment modules, and Harvey et al. (2021) for more details.

UC-DT—In the UC-DT condition, a case manager coordinated care within ACBHCS and referred each participant for a medication review and to various programs (e.g., health care, housing). After eight months in UC-DT, participants received eight sessions of TranS-C+UC.

Measures Included at Pre-Treatment Assessment Only

Sleep and Circadian Problems: Diagnoses and Subdiagnostic Symptoms—To determine whether participants met full diagnoses or subdiagnostic symptoms for sleep and circadian problems, the Duke Structured Interview for Sleep Disorders (DSISD; Edinger et al., 2004) was administered. The DSISD is a semi-structured interview designed to detect sleep and circadian problems according to the International Classification of Sleep Disorders (ICSD; American Academy of Sleep Medicine, 2014) and the DSM-5 criteria. During interviews with participants, the assessors ascertained whether each sleep and circadian problem was better explained by a different disorder (e.g., psychiatric, medical, or substance use disorder). If the sleep and circadian problem was better explained by a different disorder, a full diagnosis was not given for the sleep and circadian problem. The DSISD has demonstrated discriminant validity and reliability (kappa range: .71–.86; Edinger et al., 2009). For full diagnoses, the DSISD was clarified via self-report daily sleep diaries collected for the week preceding pre-treatment assessment. For periodic limb movement, full diagnosis was not determined, as this requires polysomnography (American Academy of Sleep Medicine, 2014).

To identify subdiagnostic symptoms, core symptoms from the DSM-5 were pre-determined for each sleep and circadian problem. A core symptom was defined as a symptom that was essential to diagnosis (e.g., endorsing nightmares for nightmare disorder). Note that when evaluating subdiagnostic symptoms, the diagnostic criterion of ‘unless better explained by another disorder’ was not included as a core symptom, because it is not central to any particular diagnosis. Based on prior subdiagnostic research, patients were categorized as ‘subdiagnostic symptoms only’ if they endorsed one or more core DSM-5 symptoms assessed by the DSISD but did not meet full diagnostic criteria (Laborde-Lahoz et al., 2015). For periodic limb movement, the core symptom was pre-identified from the DSISD rather than the DSM-5, as this disorder is not in the DSM-5.

Stratification and Mental Illness Diagnoses—Age was collected using a demographics form. Psychosis was assessed using the Mini International Neuropsychiatric Interview (MINI) (DSM-5, Version 7.0.0).

Measures Collected at All Assessments (Pre, Post, 6FU)

Primary outcome measures mirrored Harvey et al. (2021) and clinicaltrials.gov (NCT02469233). Note that in Harvey et al. (2021) and clinicaltrials.gov, secondary measures were included to assess psychosocial functioning more specifically. Secondary measures were not included in the present study, because the hypotheses could be tested with the primary measures. This decision to omit the secondary measures also served to limit Type I error associated with multiple testing.

The two exceptions to omitting secondary measures were that—to gain a fuller picture of transdiagnostic sleep and circadian functioning using multiple methods—we analyzed a) sleep/wake variables via the Sleep Health Composite and b) total sleep time variability via actigraphy (Buysse et al., 2006). The Sleep Health Composite incorporates sleep diary parameters and is proposed as a better measure of transdiagnostic sleep and circadian problems relative to individual sleep parameters (Dong et al., 2019). Total sleep time variability via actigraphy was selected for four reasons: 1) actigraphy served as an objective measure of sleep and circadian functioning, 2) variability (vs. average estimates) may be a better metric of sleep and circadian functioning in transdiagnostic samples, as regularizing total sleep time is likely to be a sleep goal across sleep and circadian problems, 3) increasing evidence suggests that total sleep time variability is associated with indicators of circadian dysregulation over and above mean total sleep time (e.g., Bei et al., 2017), and 4) total sleep time variability is thought to be a critical variable that drives exacerbation of various psychiatric symptoms (Bei et al. 2016; Gruber et al., 2011; Lemola et al., 2013), again aligning with the present study's transdiagnostic approach.

Primary Measures—The Sheehan Disability Scale (SDS) assessed functional impairment (Sheehan et al., 1996). The first three items on the SDS assess impairment in work/school, social life, and home/family responsibilities on a scale from 0–10 ('not at all' to 'extremely'). These items are summed and range from 0–30, with higher scores indicating greater impairment. The SDS has demonstrated adequate reliability and validity (Leon et al., 1996; Sheehan et al., 1996).

The DSM-5 Cross-Cutting Measure assessed general psychiatric symptoms (Narrow et al., 2013). Across 13 mental health domains, participants rate how bothered they were by a list of psychiatric symptoms from 0–4 ('not at all' to 'nearly every day'). Total scores range from 0–52, with higher scores indicating greater psychiatric severity. The measure has demonstrated good test-retest reliability and clinical utility (Clarke & Kuhl, 2014; Narrow et al., 2013).

The 8-item PROMIS—Sleep Disturbance (PROMIS-SD) assessed sleep disturbance (e.g., restlessness, sleep quality) over the past week on a scale from 1–5 ('not at all' to 'very much'; Yu et al., 2011). Scores range from 8–40. Higher scores indicate increased disturbance. This questionnaire has demonstrated adequate reliability and validity (Yu et al., 2011).

The 16-item PROMIS—Sleep Related Impairment (PROMIS-SRI) assessed sleep-related impairment during waking hours over the past week on a scale from 1–5 ('not at all' to

'very much'). The PROMIS-SRI measures perceptions of alertness, sleepiness, and tiredness (Buysse et al., 2010). Raw scores range from 16–80. Higher scores indicate increased impairment. This measure has demonstrated adequate validity (Buysse et al., 2010; Yu et al., 2011). A discussion of PROMIS T-scores can be found in Harvey et al. (2021).

Sleep/Wake Variables—Sleep and circadian problems were further assessed by actigraphy (GT9X, Actigraph) and daily sleep diaries collected for seven days prior to each assessment point. With actigraphy, variability in total sleep time was assessed, as described above. The daily sleep diary variables were analyzed for the purpose of calculating the Sleep Health Composite. Specifically, the Sleep Health Composite score (Dong et al., 2019) was defined as the sum of scores on six sleep health dimensions (each dimension dichotomized as 1 = good; 0 = poor): Regularity (midpoint fluctuation via sleep diary), Satisfaction (sleep quality question on PROMIS-SD), Alertness (daytime sleepiness question on PROMIS-SRI), Timing (mean midpoint via sleep diary), Efficiency (sleep efficiency via sleep diary) and Duration (total sleep time via sleep diary). Scores range from 0–6, with higher scores indicating better sleep health. This measure is proposed to capture the complexity of sleep problems in SMI that are covered by TranS-C. Initial validity of this measure has been established (Dong et al., 2019).

Data Analysis

Data were analyzed with Stata 16.1.

Aim 1—For Aim 1, we evaluated baseline functioning associated with number of sleep and circadian problems (Aim 1a) and diagnostic threshold of sleep and circadian problems (Aim 1b) via analysis of covariance (ANCOVA). For Aim 1a, number of sleep and circadian problems was quantified by coding each participants' number of full diagnoses and subdiagnostic symptoms of distinct sleep and circadian problems (*range*: 1–7 problems). For Aim 1b, diagnostic threshold was assessed using the process described above (see Measures) and represented by two dummy-coded variables (0 = full diagnoses only, 1 = full diagnoses with other subdiagnostic symptoms, 2 = subdiagnostic symptoms only). Significant ANCOVAs were followed up with planned pairwise comparisons for adjusted means using a t-statistic and the Tukey-Kramer correction to account for unbalanced data. Omega squared (ω^2) is reported as an effect size for ANCOVAs and can be interpreted as the proportion of variance attributed to the independent variable of interest (Field, 2013; Salkind, 2010). Participants with six comorbidities ($n = 2$) and seven comorbidities ($n = 2$) were not included due to sample size. Listwise deletion was used for missing data (Kline, 2011).

Aim 2—Random intercept multilevel models were used to compare the effects of TranS-C+UC versus UC-DT. Because randomization was stratified for psychosis and age taken at baseline, we controlled for these variables. Data were assumed to be missing at random and estimated with restricted maximum likelihood to account for sample size. All available data were used. The fixed component of the model consisted of two dummy-coded variables for time (0=pre-treatment assessment, 1=post-treatment, 2=6FU), one dummy-coded variable for treatment condition (0=UC-DT, 1=TranS-C), two time-by-treatment interaction terms,

and the variables for which we controlled (i.e., age, psychosis). The moderation models (see below) also included time-by-treatment-by-number of sleep and circadian problems interactions, with number of sleep and circadian problems scored continuously. The random component of the model consisted of a random intercept for participants and a level-1 (i.e., occasion) error term.

First, we tested whether TranS-C was associated with improved outcomes, relative to UC-DT, for individuals presenting with *specific* sleep and circadian problems. In other words, if an individual presented to treatment with insomnia, hypersomnia, a circadian rhythm disorder, periodic limb movement or restless leg syndrome, or a parasomnia, would TranS-C be a helpful treatment option for them? To test this question, participants were identified as having one or more full diagnosis or subdiagnostic symptoms of the following sleep and circadian problems: insomnia, hypersomnia, circadian rhythm disorders, periodic limb movement or restless leg syndrome, and parasomnias. Then separate multilevel models were evaluated for participants with a full diagnosis or subdiagnostic symptoms of each of these sleep and circadian problems. Participants were not excluded from a model based on comorbidities. For example, some participants endorsed insomnia and hypersomnia, and therefore were included in both models. Because of this overlap, which is common in 'real life' community settings (e.g., Hombali et al., 2019), separate models were tested for each sleep and circadian problem. This allowed us to test whether TranS-C was associated with improvements, relative to UC-DT, 'in the presence of' a given sleep or circadian problem. Second, we tested whether number of sleep and circadian problems moderated treatment outcomes. Specifically, we tested whether there was a significant three-way interaction between time, treatment, and number of sleep and circadian problems for each outcome.

Results

Demographic and clinical characteristics from pre-treatment assessment are in Table 2. Frequencies of sleep and circadian problems are available in Supplement Table 1. As seen in Table 2 and Supplement Figure 1, 121 participants (mean age=45.45 (*13.25*) years; 52.06% female, 42.98% African American or Black) began the intervention with 60 receiving UC-DT and 61 receiving TranS-C+UC. See Harvey et al. (2021) for addition details about the sample.

Aim 1: Baseline Functioning by Number and Diagnostic Threshold of Sleep and Circadian Problems

For Aims 1a and 1b, results of ANCOVAs are presented in Table 3, and pairwise comparisons are presented in Table 4. Means and standard deviations of baseline functioning by number of sleep and circadian problems are presented in Supplement Table 2. Means and standard deviations of baseline functioning by diagnostic threshold (full diagnoses, full diagnoses with other subdiagnostic symptoms, subdiagnostic symptoms only) of sleep and circadian problems are presented in Supplement Table 3. Graphs of these mean values with standard deviation and significance bars are presented in Supplement Figures 2–12.

Aim 1a: Baseline Functioning by Number of Sleep and Circadian Problems— ANCOVAs suggested significant differences in baseline functioning by number of sleep

and circadian problems, controlling for diagnostic threshold. Specifically, number of sleep and circadian problems was significantly associated with SDS, DSM-5 Cross-Cutting Measure, PROMIS-SRI, and Sleep Health Composite. For SDS, 2 or more problems vs. 1 problem and 5 problems vs. 2 problems were associated with poorer functioning. For DSM-5 Crossing-Cutting Measure, 4 problems vs. 2 problems were associated with worse psychiatric symptoms. For PROMIS-SRI, 3 or more problems vs. 1 problem and 5 problems vs. 2 problems were associated with worse sleep-related impairment. For Sleep Health Composite, 2 or more problems vs. 1 problem were associated with poorer overall sleep health.

Aim 1b: Baseline Functioning by Diagnostic Threshold—ANCOVAs suggested that there were no significant differences in baseline functioning by diagnostic threshold, accounting for number of sleep and circadian problems.

Aim 2: Outcomes for Specific Sleep and Circadian Problems and Moderation by Number of Sleep and Circadian Problems

For Aim 2, multilevel modeling results are presented in Table 5. See Supplement Table 4 for means, standard deviations, and effect sizes of outcomes at each assessment point for each specific sleep and circadian disorder. Time-by-treatment interactions, reported below, are interpretable as the difference between TranS-C+UC relative to UC-DT in mean change from pre-treatment assessment to post-treatment and from pre-treatment assessment to 6FU. Effect sizes of treatment effects for specific sleep and circadian problems are represented as '*d*' and were calculated using mean change scores (i.e., from pre- to post-treatment and pre-treatment to 6FU) and raw standard deviations from each treatment condition, based on equation 5 in Feingold, 2009).

Insomnia—For participants with full diagnoses or subdiagnostic symptoms insomnia, TranS-C+UC demonstrated reductions in SDS (b=−3.47, p=0.02, d=−0.65), DSM-5 Cross-Cutting Measure (b=−6.10, p=0.001, d=−0.66), PROMIS-SD (b=−5.79, p<0.001, d=−1.03), and PROMIS-SRI (b=−9.54, p<0.001, d=−0.85) at post-treatment. Treatment gains for TranS-C+UC were maintained through 6FU for DSM-5 Cross-Cutting Measure (b=−3.84, p=0.04, d=−0.42), PROMIS-SD (b=−4.83, p<0.001, d=−0.79), and PROMIS-SRI (b=−5.17, p=0.046, d=−0.52). For the Sleep Health Composite, TranS-C+UC exhibited improved sleep health at post-treatment (b=0.99, p=0.002, d=0.61) and to 6FU (b=0.73, p=0.02, d=0.43).

Hypersomnia—At post-treatment, for participants with full diagnoses or subdiagnostic symptoms of hypersomnia, participants in TranS-C+UC demonstrated a reduction in DSM-5 Cross-Cutting Measure (b=−6.08, p=0.008, d=−0.57), PROMIS-SD (b=−5.47, p<0.001, d=−1.00), and PROMIS-SRI (b=−9.35, p=0.001, d=−0.82). These treatment gains were maintained through 6FU for PROMIS-SD (b=−5.08, p=0.001, d=−0.98). For the Sleep Health Composite, TranS-C+UC exhibited improved sleep health at post-treatment (b=1.10, p=0.002, d=0.64) though treatment gains were not maintained through 6FU.

Circadian Rhythm Disorders—For participants with full diagnoses or subdiagnostic symptoms of circadian rhythm disorders, at post-treatment, participants in TranS-C+UC

demonstrated a reduction in PROMIS-SD (b=−6.36, p=0.007, d=−0.98) and PROMIS-SRI (b=−10.37, p=0.02, d=−1.01). Treatment gains were maintained through 6FU for both measures: PROMIS-SD (b=−7.42, p=0.001, d=−1.14) and PROMIS-SRI (b=−8.87, p=0.042, d=−0.94).

Periodic Limb Movement and Restless Leg Syndrome—For participants with full diagnoses or subdiagnostic symptoms of periodic limb movement and/or restless leg syndrome, TranS-C+UC was associated with a reduction in DSM-5 Cross-Cutting Measure (b=−7.92, p=0.009, d=−1.14) at post-treatment and PROMIS-SD (b=−5.05, p=0.02, d=−0.80) at 6FU.

Parasomnias—For participants with full diagnoses or subdiagnostic symptoms of parasomnias, at post-treatment, participants in TranS-C+UC demonstrated a reduction in DSM-5 Cross-Cutting Measure (b=−6.10, p=0.03, d=−0.81), PROMIS-SD (b=−8.16, p<0.001, d=−1.51), and PROMIS-SRI (b=−13.48, p<0.001, d=−1.29). Treatment gains for TranS-C+UC were maintained through 6FU for PROMIS-SD (b=−6.22, p=0.001, d=−1.09) and PROMIS-SRI (b=−6.81, p=0.03, d=−0.64). For the Sleep Health Composite, TranS-C+UC exhibited improved sleep health at post-treatment (b=1.48, p<0.001, d=1.07), though treatment gains were not maintained through 6FU.

Moderation by Number of Sleep and Circadian Problems—Multilevel moderation results of TranS-C+UC outcomes by number of sleep and circadian problems are presented in Table 6. Number of sleep and circadian problems did not moderate effects of TranS-C+UC at post-treatment or 6FU for any outcomes (all ps > .05).

Discussion

The present study evaluated comorbidities and treatment outcomes in the context of a transdiagnostic treatment for sleep and circadian problems delivered to individuals diagnosed with SMI in a community mental health center. At the outset, we highlight the high rates of comorbidity. Less than 15% of participants presented with a full diagnosis or subdiagnostic symptoms of a single sleep and circadian problem. In other words, the majority of participants (86.77%) had full diagnoses or subdiagnostic symptoms of at least two sleep and circadian problems (Supplement Table 2). These findings corroborate reports that comorbidity is the norm, rather than the exception, and underscore the need for research on comorbidity between sleep and circadian problems (Dalgleish et al., 2020; Hombali et al., 2019)

Aim 1a was to evaluate baseline functioning associated with number of sleep and circadian problems. When compared to a single sleep and circadian problem, participants with two or more problems endorsed greater overall impairment, psychiatric symptoms, and more sleep and circadian dysfunction at baseline. Notably, findings controlled for diagnostic threshold, meaning that *number* of problems was uniquely associated with functioning, beyond whether those problems met full diagnostic criteria.

There are two caveats worth noting for Aim 1a. First, the evidence that number of sleep and circadian problems was associated with general psychiatric symptoms was rather limited, with only one significant comparison (i.e., 4 problems vs. 2 problems). The explanation for this limited evidence is unclear. For instance, it is possible that this finding is spurious. It is also possible that different mental illnesses may have unique relationships to number of sleep and circadian problems. Future research with more specific measures of mental illness (e.g., bipolar disorder, depressive disorders) would help expand on these initial findings. Second, an exception to the pattern of findings from Aim 1a was that number of sleep and circadian problems was not associated with the actigraphy parameter of total sleep time variability. However, given the wide inclusion gates inherent to transdiagnostic research, the multi-dimensional Sleep Health Composite may be a more informative metric of sleep and circadian improvements relative to individual parameters, such as total sleep time variability (Dong et al., 2019). Indeed, individuals with two or more problems reported worse overall sleep on the Sleep Health composite than those with a single sleep and circadian problem. Together, these findings add to the growing literature that comorbidity—in this case, sleep and circadian comorbidity—is associated with more severe dysfunction (Kessler et al., 2005).

Aim 1b was to evaluate baseline functioning associated with diagnostic threshold of sleep and circadian problems (i.e., full diagnoses only, full diagnoses with other subdiagnostic symptoms, subdiagnostic symptoms only). Diagnostic threshold was not associated with poorer baseline functioning, controlling for number of sleep and circadian problems. In other words, impairment was as significant for participants with subdiagnostic symptoms as it was for participants who met full diagnostic criteria. Together, diagnostic threshold may have less of an impact on functioning than *number* of sleep and circadian problems. This explanation is consistent with evidence that subdiagnostic symptoms are associated with poor psychiatric outcomes (e.g., Balazs et al., 2013; Marangell, 2004). Clinically, these findings highlight the importance of evaluating and treating subdiagnostic symptoms and support calls for dimensional versus categorical approaches to mental illness (Cuthbert & Insel, 2013; Dalgleish et al., 2020).

Aim 2 was to evaluate outcomes of TranS-C+UC versus UC-DT for specific sleep and circadian problems. We also tested whether number of sleep and circadian problems moderated treatment effects. First, with respect to the latter, number of sleep and circadian problems did not moderate treatment outcomes. This finding should be considered in light of the high rates of comorbidity between sleep and circadian problems observed in the present trial and other psychiatric samples from the community (e.g., Sarfan et al., 2021; Hombali et al., 2019). These high rates of comorbidity underscore the need for transdiagnostic treatments that improve functioning for individuals with more than one sleep and circadian problem, like TranS-C+UC.

Second, across all models testing TranS-C+UC for individuals with specific sleep and circadian problems, TranS-C+UC relative to UC-DT was associated with significant improvements in psychiatric symptoms, sleep-related disturbance and daytime impairment, and overall sleep health by post-treatment and/or 6FU. Extending prior research on TranS-C+UC efficacy (e.g., Harvey et al., 2021), the results offer additional evidence that may

support the use of TranS-C+UC for participants with a wide range of specific sleep and circadian problems, including insomnia, hypersomnia, parasomnias, periodic limb movement and restless leg syndrome, and circadian rhythm disorders. For example, consider a patient who presents to treatment with symptoms of insomnia, hypersomnia, parasomnias, and/or restless leg syndrome. Our results suggest that TranS-C+UCT may confer clinical benefits in the presence of each of these sets of symptoms, and therefore, may be a useful treatment for this patient. Although definitive conclusions cannot be drawn due to overlap across models of participants with specific sleep and circadian problems, these results may help clinicians determine whether TranS-C+UC could be beneficial, when faced with a particular patient's presenting symptoms or diagnoses.

Taking a broader perspective, findings from Aim 2 replicate prior research demonstrating that sleep treatments improve both symptoms of comorbid mental health conditions *and* sleep and circadian functioning (Taylor & Pruiksma, 2014). Moreover, this study adds to the evidence for high rates of comorbidity (Kessler et al, 2005) and growing recognition of 'massive heterogeneity' across symptoms and comorbidities (Dalgleish et al., 2020, p. 181; Sarfan et al., 2021). Together, the results support proposals that the transdiagnostic approach may represent an efficient path to treatment in 'real world' practice settings, such as community mental health centers. Specifically, by targeting common processes and impairment associated with comorbid symptoms, transdiagnostic treatments may reduce training costs, ease provider burden, and expedite patient recovery (Mansell et al., 2009; McHugh et al., 2009)

There were two exceptions to the pattern of TranS-C outcomes. First, for participants with circadian rhythm disorders, sleep-related disruption and daytime impairment improved in TranS-C+UC relative to UC-DT, but other outcomes did not. A visual inspection of means and effect sizes for these individuals suggests an advantage for TranS-C+UC that mirrors the pattern for the other sleep and circadian problems (i.e., improvements in functional impairment, psychiatric symptoms, sleep/wake patterns, see Supplement Table 4). That said, other findings from our group suggest that the optional modules for circadian rhythm disorders were not delivered consistently for participants with circadian rhythm diagnoses (Sarfan et al., 2021), which may account for these findings. Second, for participants with periodic limb movement or restless leg syndrome, psychiatric symptoms and sleep disruption improved, but other symptoms did not. Similar to the circadian rhythm disorders, effect sizes for overall impairment, daytime sleep-related impairment, and overall sleep health were in the anticipated direction (see Supplement Table 4). However, it is possible that participants with periodic limb movement or restless leg syndrome need additional support, such as treatment modules that more specifically target their uncomfortable physical sensations. Given that few psychosocial treatments are currently recommended for periodic limb movement and restless leg syndrome (Aurora et al., 2012), this represents an exciting direction for future research.

Several limitations warrant consideration. First, our findings drew from an adequately powered parent trial (Harvey et al., 2021), and we followed multilevel modeling guidelines for sample size (McNeish & Stapleton, 2016). However, findings should be replicated and extended with larger samples. In particular, future research would benefit from larger

samples of each sleep and circadian problem without needing to 'double count' participants across models. This will be an important challenge for comorbidity research in 'real world' treatment settings, given the substantial heterogeneity across combinations of sleep and circadian problems, which can be observed in Supplement Table 1 and community samples from prior research (e.g., Hombali et al., 2019). Further, we encourage readers to focus on the effect sizes of the present results, rather the values of statistical significance, given the relatively small sample size. Second, assessors were blind to treatment condition, but participants were not, which may have influenced self-report outcomes. Third, we did not use the gold standard assessment for all sleep diagnoses. Mostly notably, we did not include polysomnography, which is an objective sleep measurement required for several sleep diagnoses, including periodic limb movement disorder. Thus, the full diagnosis could not be determined for this disorder (American Academy of Sleep Medicine, 2014). Other than subdiagnostic symptoms of periodic limb movement disorder, we did not include sleep and circadian problems that require polysomnography for diagnosis. For example, we did not include assessment of obstructive sleep apnea, which may be more common among individuals with select SMI diagnoses—particularly major depressive disorder—compared to the general population (e.g., Stubbs et al., 2015). Expanding the results of the present study to sleep and circadian problems that require polysomnography for diagnosis will be an important next step for future research. Related, we used the DSM-5 criteria to identify diagnoses and symptoms of sleep and circadian problems, except periodic limb movement disorder, which is not in the DSM-5. For some sleep and circadian problems, the symptoms and assessments methods required for diagnosis by the DSM-5 differ from other diagnostic systems, such as the ICSD-3 (American Academy of Sleep Medicine, 2014). Consequently, findings may not generalize to individuals with sleep and circadian problems who were not assessed according to the DSM-5. Fourth, subdiagnostic symptoms were not determined until after completion of the study. Assessment of subdiagnostic symptoms prior to treatment might have influenced provider decision-making regarding which TranS-C modules to administer, and which in turn, could have affected treatment outcomes. Fifth, participants in this study were individuals seeking treatment in a community mental health center. The extent to which the findings generalize to other samples in an important topic for future research.

In summary, findings from the present study add to the growing literature on comorbidity by suggesting that higher numbers of sleep and circadian problems (versus a single problem) are associated with more severe overall impairment, psychiatric symptoms, and sleep and circadian dysfunction. Moreover, diagnostic threshold (e.g., full diagnosis vs. subdiagnostic symptoms) was not associated with poorer baseline functioning. Together, results suggest that the *number* of sleep and circadian problems—versus whether those problems meet diagnostic criteria—may be more impactful for functioning. Finally, TranS-C+UC versus UC-DT was associated with improved psychosocial functioning and sleep and circadian functioning across a range of specific sleep and circadian problems (e.g., insomnia, hypersomnia, parasomnias). Treatment effects were not moderated by number of sleep and circadian problems. Thus, TranS-C+UC may be an effective, transdiagnostic clinical choice for clinicians treating individuals with SMI and sleep and circadian problems in community mental health settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Common Sleep-Circadian Problems and TranS-C Modules

Common Sleep-Circadian Problems	Treatment Module
Irregularity, difficulty winding down/waking up	Core Module 1
Daytime Impairment	Core Module 2
Unhelpful beliefs about sleep	Core Module 3
Poor sleep-efficiency	Optional Module 1
Too much time in bed	Optional Module 2
Delayed or advanced phase	Optional Module 3
Sleep-related worry	Optional Module 4
CPAP difficulties	Optional Module 5
Disruptive environments	Optional Module 6
Nightmares	Optional Module 7
Maintenance of behavior change	Core Module 4

Note. All sessions included cross-cutting modules: functional analysis, education, motivational enhancement, and goal setting.

Table 2.

Pre-treatment Assessment Demographic and Clinical Characteristics of Participants

	UC-DT (n = 60)		TranS-C (n = 61)	
Characteristic	***n***	***%***	***n***	***%***
Female	33	55.00	30	49.18
Ethnicity				
Hispanic or Latino	9	15.00	10	16.39
Not Hispanic or Latino	51	85.00	50	81.97
Missing	0	0.00	1	1.64
Race				
White	21	35.00	25	40.98
African American/Black	26	43.33	26	42.62
American Indian or Alaskan Native	4	6.67	4	6.56
Asian	5	8.33	2	3.28
Native Hawaiian/Other Pacific Islander	2	3.33	1	1.64
Missing	2	3.33	3	4.92
Education				
High school or below	22	36.67	19	31.14
Vocational school	2	3.34	9	14.76
Some college or completed college	34	56.67	30	49.18
Graduate school	2	3.34	3	4.92
Employment				
Full-time	1	1.67	1	1.64
Part-time	6	10.00	9	14.75
Unemployed	49	81.66	49	80.33
Other	4	6.67	1	1.64
Missing	0	0.00	1	1.64
MINI Diagnosis at pre-treatment (current or past)[a]				
Schizophrenia spectrum disorder	29	49.15	26	43.33
Bipolar disorder	13	22.03	21	35.00
Major depressive disorder	17	28.81	11	18.33
Any anxiety disorder	27	45.76	30	50.00
Obsessive compulsive disorder	13	22.03	9	15.00
Post-traumatic stress disorder	12	20.34	6	10.00
Substance Use Disorder	20	33.90	19	31.67
Psychotic symptoms/features	42	71.19	39	65.00
	M	**SD**	**M**	**SD**
Age (in years)	45.45	13.25	47.97	11.51
Annual personal income	$12,732	$15,547	$12,636	$9,850
Annual household income	$24,091	$27,507	$26,537	$23,576

Note.

[a]Comorbidity was common. MINI = *Mini-International Neuropsychiatric Interview*.

Table 3.

ANCOVA Results – Baseline Functioning by Diagnostic Threshold and Number of Sleep and Circadian Problems

	F-statistic	p value	ω^2
Primary Measures			
SDS			
Diagnostic threshold	F(2, 109) = 1.18	0.31	0.003
Number of problems	F(4, 109) = 6.09	< **0.001**	0.15
DSM5			
Diagnostic threshold	F(2, 110) = 2.93	0.06	0.03
Number of problems	F(4, 110) = 2.97	**0.02**	0.06
PROMIS-SD			
Diagnostic threshold	F(2, 110) = 1.69	0.19	0.01
Number of problems	F(4, 110) = 2.19	0.07	0.04
PROMIS-SRI			
Diagnostic threshold	F(2, 110) = 0.39	0.68	0.01
Number of problems	F(4, 110) = 5.08	< **0.001**	0.12
Sleep/Wake Variables			
Sleep Health Composite			
Diagnostic threshold	F(2, 110) = 0.34	0.71	0.01
Number of problems	F(4, 110) = 5.19	< **0.001**	0.13
TST variability - actigraphy			
Diagnostic threshold	F(2, 107) = 0.42	0.66	0.01
Number of problems	F(4, 107) = 0.68	0.60	0.01

Note. Omega squared (ω^2) is reported as an effect size for ANCOVAs. SDS = Sheehan Disability Scale. DSM5 = DSM-5 Cross-Cutting Measure. PROMIS-SD = Patient-Reported Outcomes Measurement Information System–Sleep Disturbance. PROMIS-SRI = Patient-Reported Outcomes Measurement Information System– Sleep-Related Impairment. TST = total sleep time.

Table 4.

Planned Pairwise Comparisons for Adjusted Means Following Significant ANCOVAs

Measures	t-statistic	p value
Primary Measures		
SDS		
2 vs. 1	t(41) = 3.23	**0.01**
3 vs. 1	t(51) = 3.99	**0.001**
4 vs. 1	t(38) = 3.84	**0.002**
5 vs. 1	t(26) = 4.85	< **0.001**
3 vs. 2	t(62) = 1.47	0.58
4 vs. 2	t(49) = 1.58	0.51
5 vs. 2	t(37) = 3.05	**0.02**
4 vs. 3	t(59) = 0.32	0.98
5 vs. 3	t(47) = 2.13	0.22
5 vs. 4	t(34) = 1.77	0.40
DSM5		
2 vs. 1	t(41) = −0.20	0.99
3 vs. 1	t(52) = 0.97	0.87
4 vs. 1	t(38) = 2.15	0.21
5 vs. 1	t(26) = 1.53	0.55
3 vs. 2	t(63) = 1.69	0.44
4 vs. 2	t(49) = 1.69	**0.01**
5 vs. 2	t(37) = 2.18	0.20
4 vs. 3	t(60) = 2.05	0.25
5 vs. 3	t(48) = 1.02	0.85
5 vs. 4	t(34) = −0.57	0.98
PROMIS-SRI		
2 vs. 1	t(41) = 2.48	0.10
3 vs. 1	t(52) = 3.44	**0.007**
4 vs. 1	t(38) = 3.66	**0.004**
5 vs. 1	t(26) = 4.27	<**0.001**
3 vs. 2	t(63) = 1.69	0.45
4 vs. 2	t(49) = 2.21	0.18
5 vs. 2	t(37) = 3.05	0.02
4 vs. 3	t(60) = 0.84	0.92
5 vs. 3	t(48) = 1.97	0.29
5 vs. 4	t(34) = 1.23	0.74
Sleep/Wake Variables		
Sleep Health Composite		
2 vs. 1	t(41) = −3.33	**0.010**
3 vs. 1	t(52) = −3.76	**0.003**
4 vs. 1	t(38) = −3.91	**0.001**

Measures	t-statistic	p value
5 vs. 1	t(26) = −4.38	< **0.001**
3 vs. 2	t(51) = −1.00	0.86
4 vs. 2	t(49) = −1.55	0.53
5 vs. 2	t(37) = −2.35	0.14
4 vs. 3	t(60) = −0.77	0.94
5 vs. 3	t(48) = −1.75	0.41
5 vs. 4	t(34) = −1.08	0.82

Note. The number of problems and diagnostic threshold compared via planned pairwise t-tests is displayed in the format: x vs. y (e.g., 2 vs. 1 = 2 problems compared with 1 prolem; full vs. sub = full diagnoses only compared with subdiagnostic symptoms only). Significant p-values are bolded. Tukey-Kramer's correction was used to account for unbalanced data. Full = participants with full diagnoses only. Full-sub = participants with full diagnoses and other subdiagnostic symptoms. Sub = participants with subdiagnostic symptoms only. SDS = Sheehan Disability Scale. DSM5 = DSM-5 Cross-Cutting Measure. PROMIS-SD = Patient-Reported Outcomes Measurement Information System–Sleep Disturbance. PROMIS-SRI = Patient-Reported Outcomes Measurement Information System– Sleep-Related Impairment. TST = total sleep time.

Table 5.

Multilevel Modeling – Outcomes for Specific Sleep and Circadian Problems

	Treatment condition effect at PRE			Treatment condition effect at POST			Treatment condition effect at 6FU		
	coef.	*SE*	*p*	*coef.*	*SE*	*p*	*coef.*	*SE*	*p*
Insomnia (*n* = 113)									
SDS	−2.26	1.42	0.11	−3.47	1.52	**0.02**	−1.60	1.51	0.29
DSM5 Cross-Cutting Measure	−0.60	1.92	0.75	−6.10	1.91	**0.001**	−3.84	1.90	**0.04**
PROMIS-SD	−1.07	1.32	0.42	−5.79	1.38	**<.001**	−4.83	1.38	**<.001**
PROMIS-SRI	−3.63	2.55	0.16	−9.54	2.61	**<.001**	−5.17	2.59	**0.046**
TST variability - Actigraphy	−7.43	15.65	0.64	6.07	18.82	0.75	−2.37	18.80	0.90
Sleep Health Composite	0.20	0.27	0.46	0.99	0.32	**0.002**	0.73	0.31	**0.02**
Hypersomnia (*n* = 85)									
SDS	−1.06	1.67	0.53	−3.21	1.67	0.06	−0.92	1.66	0.58
DSM5 Cross-Cutting Measure	0.62	2.37	0.79	−6.08	2.28	**0.008**	−3.32	2.26	0.14
PROMIS-SD	−0.56	1.57	0.72	−5.47	1.54	**<.001**	−5.08	1.52	**0.001**
PROMIS-SRI	0.68	3.11	0.83	−9.35	2.85	**0.001**	−5.54	2.82	0.050
TST variability - Actigraphy	0.52	19.80	0.98	−10.56	24.26	0.66	10.36	24.18	0.67
Sleep health composite	0.07	0.32	0.83	1.10	0.36	**0.002**	0.59	0.35	0.10
Circadian Rhythm Disorders (*n* = 41)									
SDS	−1.57	2.49	0.53	−2.11	2.60	0.42	−4.29	2.57	0.10
DSM5 Cross-Cutting Measure	1.10	3.26	0.74	−5.90	3.18	0.06	−3.36	3.14	0.28
PROMIS-SD	0.09	2.33	0.97	−6.36	2.36	**0.007**	−7.42	2.32	**0.001**
PROMIS-SRI	−0.25	4.48	0.96	−10.37	4.41	**0.02**	−8.87	4.35	**0.042**
TST variability - Actigraphy	−17.64	32.91	0.59	20.18	36.72	0.58	32.34	36.23	0.37
Sleep health composite	0.37	0.42	0.41	1.12	0.59	0.06	0.71	0.59	0.23
Periodic Limb Movement and/or Restless Leg Syndrome (*n* = 45)									
SDS	−2.33	2.39	0.33	−2.06	2.27	0.36	−3.23	2.20	0.14
DSM5 Cross-Cutting Measure	−3.10	2.84	0.28	−7.92	3.02	**0.009**	−5.29	2.92	0.07
PROMIS-SD	−1.86	2.27	0.41	−2.98	2.29	0.19	−5.05	2.22	**0.02**
PROMIS-SRI	−4.29	4.60	0.35	−4.34	4.26	0.31	−6.90	4.12	0.09
TST variability - Actigraphy	−2.65	26.03	0.92	29.12	30.84	0.35	4.40	29.82	0.88
Sleep health composite	0.29	0.44	0.51	0.30	0.54	0.59	0.88	0.53	0.10
Parasomnia (*n* = 57)									
SDS	−3.03	1.83	0.10	−2.53	1.98	0.20	−1.69	1.97	0.39
DSM5 Cross-Cutting Measure	−0.93	2.48	0.71	−6.10	2.81	**0.03**	−3.97	2.80	0.16
PROMIS-SD	0.88	1.82	0.63	−8.16	1.88	**<.001**	−6.22	1.87	**0.001**

	Treatment condition effect at PRE			**Treatment condition effect at POST**			**Treatment condition effect at 6FU**		
	coef.	***SE***	***p***	***coef.***	***SE***	***p***	***coef.***	***SE***	***p***
PROMIS-SRI	−4.66	3.14	0.14	−13.48	3.18	**<.001**	−6.81	3.17	**0.032**
TST variability - Actigraphy	−1.14	19.61	0.95	−5.66	25.2	0.82	−39.30	24.89	0.11
Sleep health composite	−0.12	0.34	0.72	1.48	0.40	**<.001**	0.36	0.40	0.36

Note. Parameters presented are the time-by-treatment interactions, interpreted as the difference between TranS-C+UC relative to UC-DT in mean change from pre-treatment assessment to post-treatment and from pre-treatment assessment to 6FU. PRE = pre-treatment assessment. POST = post-treatment assessment. 6FU = 6-month follow-up assessment. SDS = Sheehan Disability Scale. DSM5 = DSM-5 Cross-Cutting Measure. PROMIS-SD = Patient-Reported Outcomes Measurement Information System–Sleep Disturbance. PROMIS-SRI = Patient-Reported Outcomes Measurement Information System–Sleep-Related Impairment. TST variability – Actigraphy = total sleep time variability measured by actigraphy.

Table 6.

Multilevel Modeling Moderation 3-Way Interactions - Time by Treatment by Number of Sleep and Circadian Problems

	3-Way Interaction at POST			3-Way Interaction at 6FU		
	coef.	*SE*	*p*	*coef.*	*SE*	*p*
SDS	1.75	1.12	0.12	−0.27	1.11	0.81
DSM5 Cross-Cutting Measure	0.84	1.45	0.56	0.47	1.43	0.74
PROMIS-SD	−0.42	1.06	0.69	−0.37	1.05	0.73
PROMIS-SRI	0.10	1.96	0.96	−0.30	1.93	0.88
TST variability - Actigraphy	0.74	15.12	0.96	8.43	14.93	0.57
Sleep Health Composite	0.29	0.24	0.23	−0.03	0.24	0.89

Note. Parameters presented are the 3-way interactions between time, treatment, and number of sleep and circadian problems. POST = post-treatment assessment. 6FU = 6-month follow-up assessment. SDS = Sheehan Disability Scale. DSM5 = DSM-5 Cross-Cutting Measure. PROMIS-SD = Patient-Reported Outcomes Measurement Information System–Sleep Disturbance. PROMIS-SRI = Patient-Reported Outcomes Measurement Information System–Sleep-Related Impairment. TST variability – Actigraphy = total sleep time variability measured by actigraphy.