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A randomized controlled trial of the Transdiagnostic Intervention for Sleep and Circadian Dysfunction (Trans-C) to improve serious mental illness outcomes in a community setting

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Abstract

Objective: To determine if the Transdiagnostic Intervention for Sleep and Circadian Dysfunction (Trans-C) improves functional impairment, psychiatric symptoms and sleep and circadian functioning.

Method: Adults diagnosed with serious mental illness (SMI) and sleep and circadian dysfunction ($N=121$) were randomly allocated to Trans-C plus usual care (Trans-C+UC; $n=61$; 8 individual weekly sessions) or 6-months of Usual Care followed by Delayed Treatment with Trans-C (UC-DT; $n=60$). Schizophrenia (45%) and anxiety (47%) disorders were common. Blind assessments were conducted pre-treatment, post-treatment and 6 months later (6FU). The latter two were the post-randomization points of interest. The location was Alameda County Behavioral Health Care Services (ACBHCS), a Community Mental Health Center (CMHC) in California.

Results: For the primary outcomes, relative to UC-DT, Trans-C+UC was associated with reduction in functional impairment ($b=-3.18$, $p=0.025$, $d=-0.58$), general psychiatric symptoms ($b=-5.88$, $p=0.001$, $d=-0.64$), sleep disturbance ($b=-5.55$, $p<0.0001$, $d=-0.96$) and sleep-related impairment ($b=-9.14$, $p<0.0001$, $d=-0.81$) from pre-treatment to post-treatment. These effects were maintained to 6-month follow-up (6FU) ($d=-0.42-0.82$), except functional impairment ($d=-0.37$). For the secondary outcomes, relative to UC-DT, Trans-C+UC was associated with improvement in sleep efficiency and on the Sleep Health Composite score from pre-treatment to

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6FU. TranS-C+UC was also associated with reduced total wake time and waketime variability from pre-treatment to post-treatment, as well as reduced hallucinations and delusions, bedtime variability, and actigraphy measured waking activity count variability from pre-treatment to 6FU.

Conclusions: A novel transdiagnostic treatment, delivered within a CMHC setting, improves selected measures of functioning, symptoms of comorbid disorders, and sleep and circadian outcomes.

Keywords

Transdiagnostic; sleep; circadian; serious mental illness; dissemination; community mental health

Sleep and circadian dysfunction contribute to vicious cycles of escalating symptoms and functional deficits in persons diagnosed with a serious mental illness (SMI). SMI is operationalized according to Public Law 102–321 and previous research (Kessler et al., 2003; Wang, Demler, & Kessler, 2002) as the presence, for 12-months, of at least one DSM mental disorder that leads to substantial interference with one or more major life activities. A range of sleep and circadian problems, including insomnia, hypersomnia, advanced and delayed phase, sleep continuity problems and irregular sleep-wake schedules are commonly comorbid with SMI (Baglioni et al., 2016). These problems often persist even when the SMI is treated (López, Lancaster, Gros, & Acierno, 2017) and they predict and predate SMI symptom onset and escalation (Hertenstein et al., 2018). Moreover, insufficient sleep exacerbates emotion regulation difficulty, poor problem solving, difficulty with cognitive functioning, and behaviors like impulsivity (Krause et al., 2017). Taken together, there is a need for treatment approaches that address the complexity of real-life sleep and circadian problems in mental illness. The Transdiagnostic Sleep and Circadian Intervention (TranS-C) (Harvey & Buysse, 2017) has been proposed to address the need for one short protocol to address the broader range of sleep and circadian dysfunction experienced by SMI patients. TranS-C is grounded in basic science and draws on cognitive behavior therapy for insomnia (CBT-I)—the first-line treatment for insomnia (Qaseem, Kansagara, Forcica, Cooke, & Denberg, 2016), which effectively treats insomnia across psychiatric disorders and often the comorbid disorder (Geiger-Brown et al., 2015)—along with Interpersonal and Social Rhythm Therapy (Frank et al., 2005), Chronotherapy (Wirz-Justice, Benedetti, & Terman, 2009) and Motivational Interviewing (Miller & Rollnick, 2002). TranS-C is transdiagnostic in two ways: It addresses a range of sleep and circadian problems across a range of SMI.

TranS-C is likely to be highly disseminable due to the substantial cost advantage to training providers in one treatment protocol that covers multiple problems (McHugh & Barlow, 2010). Further, an important gap in knowledge is the performance of treatments in routine practice settings as most treatment research is conducted in research settings. CBT-I has been effectively delivered in a range of real world settings (Espie et al., 2008; Karlin, Trockel, Taylor, Gimeno, & Manber, 2013). The present study was conducted to extend these findings by delivering TranS-C in Community Mental Health Centers (CMHCs). CMHCs are critical settings as they are major, publicly funded providers of treatment for SMI. They provide for the poorest and most underserved members of the community who experience high rates of comorbidity and complexity (Drake et al., 2001). As such, transdiagnostic treatments, like TranS-C, are appropriate as they target processes that

underpin multiple disorders and afford treatment for a greater heterogeneity of clinical presentations.

The Sleep Health Framework (Buysse, 2014) underpins and guides TranS-C. This approach encourages sleep improvement along six dimensions that have been linked to mental and physical health outcomes (Buysse, 2014). The dimensions are: *regularity* of sleep and waking up; *satisfaction* with sleep or sleep quality; *alertness* during waking hours or daytime sleepiness; appropriate *timing* of the patient's sleep within the 24-hour day; *sleep efficiency*, i.e., the ability to sleep for a large percentage of the time in bed, as indicated by ease of falling asleep at the beginning of the night and the ease of returning to sleep after awakenings across the night; and *sleep duration* which is the total amount of sleep obtained by the patient per 24 hours. (note the acronym RUSATED, i.e., Has your sleep “filled up” your emotional, cognitive, and physical need to sleep?). TranS-C aims to promote sleep health along these six dimensions.

As described in the study protocol (Harvey et al., 2016), the aim was to evaluate the effects of TranS-C plus usual care (TranS-C+UC) vs. Usual Care followed by Delayed Treatment with TranS-C (UC-DT) on *functional impairment*, *general psychiatric symptoms* and *sleep and circadian function* in participants receiving treatment for SMI in a CMHC. The hypothesis tested is that TranS-C+UC will be superior to UC-DT at post-treatment and 6-month follow-up (6FU).

Method

Study Design

Adults ($N=121$) were randomly assigned, in a 1:1 parallel group design, to TranS-C plus Usual Care (TranS-C + UC; $n=61$) or Delayed Treatment with TranS-C following 6-months of Usual Care (UC-DT; $n=60$) (see Figure 1 for the CONSORT flowchart). Randomization was stratified by lifetime presence of a psychotic disorder (yes, no) and age (49 and under, 50+). Participants completed a battery of measures at pre-treatment, post-treatment (9–14 weeks later) and 6FU. Assessors were blinded to treatment allocation. A project coordinator conducted randomization after each eligibility assessment was completed. The Committee for the Protection of Human Subjects approved the study. A Data Safety and Management Committee reviewed the progress and safety of study procedures twice per year. No adverse events were reported.

Participants and Setting

Adults who met criteria for SMI and sleep and circadian dysfunction were recruited from multiple sites within Alameda County Behavioral Health Care Services (ACBHCS), the CMHC for Alameda County, California. Participants were referred via case managers and psychiatrists, and recruited via advertising in clinic waiting rooms and giving presentations. 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-defined mental disorder that leads 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: 1) Age 18+ years; 2) English language fluency; 3) presence of at least one DSM-5 mental disorder for 12 months; 4) one or more sleep or circadian problems for 3 months assessed with the Sleep and Circadian Problems Interview; 5) having a guaranteed bed to sleep in for 3 months; 6) receiving care for SMI at ACBHCS; and 6) consenting to regular communications between research team and psychiatrist and/or case manager. Sleep and circadian problems included: taking 30 mins to get to sleep 3 or more nights per week, waking in the middle of the night for 30 minutes 3 or more nights per week, obtaining <6 hours of sleep per night 3 or more nights per week, obtaining >9 hours of sleep per 24 hour period (i.e., nighttime sleep plus daytime napping) 3 or more nights per week, having more than 2.78 hours of variability in sleep-wake schedule across one week which was selected based on mean variability in total sleep time across a week in prior research (Gruber et al., 2009) and sleeping at a bedtime later than 2 am on 3 or more nights per week.

Exclusion criteria: 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. As individuals with sleep apnea and periodic limb movement disorder often have comorbid insomnia and poor sleep habits, and can benefit from CBT-I (Edinger et al., 1996; Sweetman et al., 2019), they were included. 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.

Measures

The assessors were blind to treatment allocation. The process of ensuring reliability of the assessments was carefully managed. First, a multi-step training process was required for each assessor including a classroom training session, mock interviews, scoring of tapes of real participant interviews and then shadowing and being shadowed by a certified assessor who fully scores the assessment. For the latter two steps the trainee has to achieve an 80% match on symptoms and 100% on diagnoses. Also, senior team members were closely involved in solving diagnostic dilemmas.

In addition to demographics, the following outcomes were assessed.

Primary Outcomes.—Functional Impairment was assessed with the *Sheehan Disability Scale* (SDS) (Sheehan, Harnett-Sheehan, & Raj, 1996a). The SDS assesses mood- and sleep-related impairment (Sheehan et al., 1998). The SDS evaluates the extent to which work/school, social life, and home/family responsibilities are impaired on a 0–10 ('not at all' to 'extremely') scale. The SDS has been found to have adequate reliability and validity in multiple studies (Leon, Olfson, Portera, Farber, & Sheehan, 1997; Leon, Shear, Portera, & Klerman, 1992; Sheehan, Harnett-Sheehan, & Raj, 1996b). The 3 items were averaged to assess global functional impairment (0 not impaired to 10 highly impaired).

The *DSM-5 Cross-Cutting Measure* (DSM-5) was included as a measure of general psychiatric symptoms (Narrow et al., 2013). This measure includes 23-items to assess mental health domains that are critical across psychiatric diagnoses (Clarke & Kuhl, 2014; Narrow et al., 2013). It measures impairment in the following domains: depression, anger, mania, somatic symptoms, suicidal ideation, psychosis, sleep problems, memory, repetitive thoughts and behaviors, dissociation, personality functioning, and substance use. Individuals report how much each domain has bothered them in the last two weeks on a 0–4 scale ('not at all' to 'nearly every day'). Each item is rated on a 5-point scale, with higher scores indicating more severe impairment. The measure has demonstrated good test-retest reliability and clinical usefulness (Clarke & Kuhl, 2014; Narrow et al., 2013).

Sleep and circadian function was assessed with the *PROMIS–Sleep Disturbance (PROMIS–SD)* (Yu, Buysse, Germain, & Moul, 2012) and the *PROMIS–Sleep-Related Impairment (PROMIS–SRI)* (Yu et al., 2012). The PROMIS–Sleep Disturbance (PROMIS–SD) (Yu et al., 2012) was developed based on the PROMIS–Sleep Disturbance item bank. The 8-item short version assesses sleep disturbance over the past seven days, including restlessness, sleep quality, ability to fall and stay asleep, and refreshment following sleep using a 1–5 scale ('not at all' or 'never' to 'very much' or 'always'). Scores range from 8 to 40, with higher scores indicating increased disturbance (Yu et al., 2012). The PROMIS-SD has demonstrated reliability and validity (Yu et al., 2012).

We administered the 16-item version of the PROMIS–Sleep Related Impairment (PROMIS–SRI) questionnaire in which participants rate difficulties during wakeful hours associated with sleep problems over the last week on a 5-point scale (Yu et al., 2012). The PROMIS–SRI measures perceptions of alertness, sleepiness and tiredness within the overall context of sleep-wake function, but does not directly assess cognitive, affective, or performance impairments. Scores range from 16 to 80, with higher scores indicating increased disturbance (Yu et al., 2012). The PROMIS–SRI has also demonstrated adequate validity when compared to other measures of daytime symptoms such as the Epworth Sleepiness Scale (Yu et al., 2012).

Secondary Outcomes.—General psychiatric symptoms were more specifically assessed by the *Quick Inventory of Depressive Symptoms (QIDS)* (Rush et al., 2003), *Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)* (Group, 2002) and/or the *Psychotic Symptoms Rating Scales (PSYRATS)* (Haddock, McCarron, Tarrier, & Faragher, 1999).

The self-report version of the QIDS is a widely-used 16-item instrument assessing depressive symptoms. Each item is rated on a four-point scale from 0–3, with higher scores indicating greater symptom severity. The measure has demonstrated good reliability and validity (Rush et al., 2003).

The ASSIST evaluates psychoactive substance use and measures related impairment (Group, 2002). ASSIST measures lifetime substance use as well as frequency of use and related problems within the past three months. Frequency of use, substance dependence, and related health, social, legal, financial, and employment problems in the past three months are rated

on a 5-point scale ('never' to 'daily of almost daily'). Problems with family and friends caused by substance use and failed attempts to cut down or quit substance use are measured on a 3-point scale ('no, never', 'yes, in the past 3 months', 'yes, but not in the past 3 months'). ASSIST has good reliability and clinical feasibility (Group, 2002).

The PSYRATS is a semi-structured interview designed to assess the subjective characteristics of hallucinations and delusions (Haddock et al., 1999). Each of the 17-items is rated on a 5-point scale (0–4). The PSYRATS has good reliability and validity in first episode samples and complimentary existing measures (Drake, Haddock, Tarrier, Bentall, & Lewis, 2007).

Functional impairment was further assessed with the self-administered version of the *World Health Organization Disability Assessment Schedule (WHODAS) 2.0* and the 4-question 'Healthy Days' core module (Moriarty, Zack, & Kobau, 2003).

The World Health Organization Disability Assessment Schedule (WHODAS) 2.0 is a 36-item measure that assesses disability in adults ages 18 years and older. It assesses disability across six domains on a scale from 1–5 ('none' to 'extreme or cannot do'). Each item on the self-administered version of the WHODAS-2.0 asks the individual to rate how much difficulty he or she has had in specific areas of functioning during the past 30 days (World Health Organization, 2012). The WHODAS 2.0 possesses strong psychometric properties and provides a global disability score as well as six domain scores: cognition, mobility, self-care, getting along with others, participation in society, and life activities (Konecky, Meyer, Marx, Kimbrel, & Morissette, 2014).

The 'Healthy Days' core module was developed by the Centers for Disease Control and Prevention to assess health related quality of life and is a 4-item measure. Health related quality of life was defined as "perceived physical and mental health over time." This measure asks about self-rated general health and the number of recent days when a person was physically unhealthy, mentally unhealthy, or limited in usual activities. A summary measure combines physically and mentally unhealthy days. An "unhealthy days" summary measure based on the second and third questions and estimates the overall number of recent days when physical or mental health was not good. This measure is the brief, validated and is based on a clear and explicit definition (Moriarty et al., 2003).

Sleep and circadian function was further assessed with the *daily sleep diary* and *actigraphy* (GT9X Link, ActiGraph), collected for 7 days at each assessment point. The daily sleep diary outcomes were mean and variability in sleep efficiency (total sleep time/time in bed \times 100), total sleep time, total wake time, bedtime and waketime. Trained research assistants collected the sleep diary by phone each day. Times were selected after, but as close as possible to, rise time. Outcomes analyzed from actigraphy include the mean and variability for total sleep time and total wake time, as well as waking activity count. See the Supplement for further information on scoring.

To capture the complexity of the sleep problems in SMI, we calculated a Sleep Health Composite score (Dong, Martinez, Buysse, & Harvey, 2019), defined as the sum of scores on 6 sleep health dimensions (Buysse, 2014) (each dimension was dichotomized such that

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 7-day sleep diary) and Duration (total sleep time via 7-day sleep diary). Higher scores indicate better sleep health. This measure is proposed to capture the complexity of the sleep problems covered by TranS-C. Initial validity of this measure has been established (Buysse, 2014).

Measures included at pre-treatment assessment only.—The Mini-International Neuropsychiatric Interview (MINI) (DSM-5, Version 7.0.0 including Schizophrenia and Psychotic Disorders) was included as an evaluation of the presence of current and past SMI. The MINI was developed to meet the need for a simple, short and accurate structured psychiatric interview. Screening questions are used to initially rule out the presence of mental health disorders. Positive responses to screening questions prompt further probing into severity and disability caused by the disorder. The MINI has demonstrated good test retest reliability ($\kappa > .88$) and validity (Lecrubier et al., 1997; Sheehan et al., 1998).

The diagnostic measure for sleep disorders was the *Duke Structured Interview for Sleep Disorders (DUKE)* (Edinger et al., 2009). The DSISD is a clinical semi-structured interview designed to detect the presence of a range of sleep and circadian disorders according to both the International Classification of Sleep Disorders (ICSD) and the Diagnostic and Statistical Manual of Mental Disorders criteria. Disorders assessed include insomnia, hypersomnia, circadian phase disorders, and multiple parasomnias. Each diagnostic criteria is represented as an independent question. At the end of the interview, participant reported symptomatology for each diagnostic criteria is used to determine a final diagnosis for that disorder: absent, subthreshold, or threshold. The DSISD has demonstrated discriminant validity and high reliability (κ values range from .71 to .86). Diagnoses were clarified via a review of a 7-day *daily sleep diary*.

Sleep/insomnia history was obtained with the *Sleep and Circadian Problems Interview* (Morin, 1993), to assess inclusion/exclusion criteria. To improve our ability to identify obstructive sleep apnea, we supplemented the DUKE with *STOP-BANG* (Farney, Walker, Farney, Snow, & Walker, 2011), which is an 8-item screen. Both measures are well validated and widely used. Those suspected to have another sleep disorder were referred for non-study evaluation/treatment and were *not* excluded.

A Medication Tracking Log was administered at each assessment. Treatment credibility/expectancies were assessed after Session 2 via the *Credibility/Expectancy Questionnaire* (Deville & Borkovec, 2000).

Treatments.

TranS-C—TranS-C was administered by masters' level therapists, hired within the University of California, Berkeley, who traveled between the ACBHCS clinic sites. Clinicians attended a one-day workshop, used a manual, and received weekly supervision. Usual care was administered by CMHC providers.

The average number of 50-minute sessions attended was 8. Up to 12 sessions could be provided but this was rarely needed. TranS-C includes four cross-cutting modules featured in every session (functional analysis, education, behavior change and motivation, and goal-setting), four core modules that apply to the vast majority of participants (establishing regular sleep-wake times including learning a wind-down and wake-up routine, improving daytime functioning, correcting unhelpful sleep-related beliefs, and maintaining behavior change), and seven optional modules used less commonly, depending on the needs of each participant (improving sleep efficiency, reducing time in bed, dealing with delayed or advanced phase, reducing sleep-related worry/vigilance, promoting compliance with CPAP/exposure therapy for claustrophobic reactions to CPAP, negotiating sleep in a complicated environment, and reducing nightmares). Core and optional modules can be delivered in any sequence and are customized to the participant based on their presentation and goals for treatment (see Table 4 in Supplement for a summary).

Sessions were audio recorded. TranS-C treatment integrity was evaluated with the Cognitive Therapy Rating Scale (CTRS); a score of 40 is generally regarded as competent delivery (Young & Beck, 1980). A checklist of TranS-C elements was used to rate the presence/absence of treatment elements for a random subset of tapes (Gumport, Yu, Mullin, Mirzadegan, & Harvey, 2020).

How do TranS-C and CBT-I compare? TranS-C incorporates the key tenets and procedures of CBT-I. However, it also incorporates advances in knowledge from other sleep medicine approaches to address the broader range of sleep and circadian dysfunctions commonly experienced in SMI. Relatedly, poor sleep efficiency is often a treatment target for SMI patients. This calls for stimulus control and sleep restriction. However, a notable proportion of SMI patients exhibit sleep efficiency >85%, or their sleep efficiency is corrected by regularizing bed and wake times (Kaplan & Harvey, 2013). An additional issue is that stimulus control and sleep restriction can involve partial sleep deprivation. As sleep deprivation can trigger SMI relapse (Colombo, Benedetti, Barbini, Campori, & Smeraldi, 1999), in certain cases there are safety concerns.

UC-DT.—We carefully considered the choice of comparison condition before deciding on UC-DT. Our choice to compare TranS-C to UC-DT was preferred by our community partners and aimed to strike a balance between (a) including a comparison group to demonstrate the effectiveness of TranS-C in community settings; this information is critical to determining the potential of TranS-C for broader dissemination; (b) ensuring that *all* participants receive what we hypothesize to be an active treatment (TranS-C); and (c) maximizing efficiency in terms of study duration, budget, and participants' time investment. Notably, usual care has been used as the comparison group in several influential studies (Craske et al., 2011; Daumit et al., 2013; Weisz et al., 2012).

UC-DT was conducted within ACBHCS, involved a case manager coordinating care and referring each client for a medication review and to various programs (e.g., health care, housing, vocational, 'hearing voices' group). After 8 months in UC-DT, the participants received 8 sessions of TranS-C.

Trial registration

We report the primary and secondary outcomes listed in the [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02469233) protocol (NCT02469233). This was updated on December 19, 2019 to remove nap timing and duration via sleep diary because naps were inconsistently reported and the data quality was poor.

Data Analysis

Sample size ($N=120$) was determined assuming a medium effect size across outcomes based on prior literature (Espie et al., 2008; Harvey et al., 2015), with significance of 0.05, and power of 80%. The final sample was 121 because one eligible participant was already in the ‘assessment pipeline’ at the end of the study. One prior analysis was conducted for the purpose of a grant application and conference presentation in July 2018 (75% of the data had been collected and entered).

Data were analyzed using Stata 15. Analyses were adjusted for the stratification factors (age, lifetime presence of a psychotic disorder). Intent-to-treat analysis was performed. The endpoints (treatment effects of interest) are changes comparing TranS-C vs. UC-DT on the primary and secondary outcomes from pre-treatment to post-treatment and from pre-treatment to 6FU. Multilevel modeling, with maximum likelihood estimation and the assumption of missing at random, was used to examine the outcome variables, all modeled as continuous outcome variables. The fixed component included stratification factors, dummy-coded indicator for time (0=pre, 1=post, 2=6FU), an indicator for treatment condition (0=UC-DT, 1=Immediate TranS-C+UC), and a time-by-treatment interaction term. The random part included a subject-specific random intercept and a time- and subject-specific error term. A significant treatment-by-time interaction is the treatment effect of interest, and is interpreted as the difference between TranS-C+UC vs. UC-DT in mean change (for a given outcome variable) from pre-treatment to post-treatment and to 6FU. The Benjamini-Hochberg procedure (Benjamini & Hochberg, 1995) was used to correct for multiple testing for confirmatory analyses on the primary outcomes (Moyé, 2008) (i.e., TranS-C+UC effects on each of the 4 primary outcomes from pre-treatment to post-treatment and to 6FU). Assuming a 5% false discovery rate, all p values remain significant compared to the corresponding Benjamini-Hochberg critical values.

Results

Participant Characteristics

Dropout rates were 1.7% (2 participants) before session 1, 9.9% (12 participants) between session 1 and post-treatment assessment, and 0.8% (1 participant) dropped out between post and 6FU. Attrition rates were higher in TranS-C than UC-DT during treatment phase (16.9% in TranS-C; 3.3% in UC-DT; $X^2=6.04$, $df=1$, $p=0.001$), but not significantly different prior to Session 1 (3.3% in TranS-C; 0% in UC-DT; $X^2=2.00$, $df=1$, $p=0.16$) or at 6FU (13.1% in TranS-C; 5.0% in UC-DT; $X^2=2.38$, $df=1$, $p=0.12$). Relative to completers, participants who did not begin treatment or who dropped out were not significantly different on gender ($X^2=0.09$, $df=1$, $p=0.76$), age group (above or below 50 years; $X^2=2.15$, $df=1$, $p=0.14$) or

psychosis status ($X^2=0.01$, $df=1$, $p=0.94$). Table 1 indicates the two treatment conditions did not differ on baseline variables.

Primary Outcomes

Descriptives are in Table 2. Multilevel modeling results are in Table 3. See Figure 2 for graphical presentation. There was no group difference between TranS-C+UC and UC-DT on any of the outcome variables at pre-treatment.

From pre-treatment to post-treatment, TranS-C+UC had significant effects on all four primary outcomes, relative to UC-DT. Specifically, participants in TranS-C+UC, relative to UC-DT, exhibited a reduction in SDS ($b=-3.18$, $p=0.025$), DSM-5 cross-cutting symptoms ($b=-5.88$, $p=0.001$), PROMIS-SD ($b=-5.55$, $p<0.0001$), and PROMIS-SRI ($b=-9.14$, $p<0.0001$). Treatment gains for TranS-C+UC, relative to UC-DT, were maintained through 6FU for DSM-5 cross-cutting symptoms ($b=-3.90$, $p=0.03$), PROMIS-SD ($b=-4.92$, $p<0.0001$), and PROMIS-SRI ($b=-5.37$, $p=0.027$), but not for SDS. See Supplement for a discussion and presentation of PROMIS T scores.

Secondary Outcomes

Descriptive statistics are in Table 2. Multilevel modeling results are in Table 3. Relative to UC-DT, TranS-C+UC had reduced PSYRATS scores from pre-treatment to 6FU ($b=-17.52$, $p=0.02$). For sleep diary, TranS-C+UC had improved sleep efficiency from pre-treatment to post-treatment ($b=5.68$, $p=0.03$) and 6FU ($b=5.89$, $p=0.03$), relative to UC-DT. Relative to UC-DT, TranS-C+UC showed reduced total wake time mean ($b=-39.33$, $p=0.04$) and reduced wake time variability ($b=-0.39$, $p=0.047$) from pre-treatment to post-treatment, and earlier bedtime from pre-treatment to 6FU ($b=-0.71$, $p=0.04$). For actigraphy, TranS-C+UC showed significantly reduced variability in waking activity count ($b=-0.27$, $p=0.02$) from pre-treatment to 6FU. TranS-C+UC did not show advantage over UC-DT on other outcomes.

For the Sleep Health Composite, TranS-C+UC exhibited improved sleep health from pre-treatment to post-treatment ($b=0.91$, $p=0.002$) and to 6FU ($b=0.64$, $p=0.03$), relative to UC-DT.

Treatment Integrity, Credibility and Fidelity

CTRS ($n=203$ recordings, $M=51.08$, $SD=5.66$, 98.5% 40 or over) indicate that TranS-C+UC was delivered with fidelity. Coding of a random subset of patients with no missing recordings ($n=19$; 31.15% of TranS-C participants) indicated that all 8 sessions of recordings for each patient were coded ($n=152$ sessions). 94.74% received all 4 cross-cutting modules (100% received functional analysis, education, and motivational enhancement). 36.84% received all 4 core modules (100% Core Module 1, 68.42% Core Module 2, 57.89% Core Module 3, 100% Core Module 4). 100% received at least 1 optional module. No non-TranS-C elements were coded.

Medications

At study entry, 90/121 (74.4%) were taking prescription SMI medications and 16/121 (13.2%) were taking sleep medications. The mean \pm SD (median) number of medications per participant was 2.80 \pm 1.41.

When considering each medication for each participant separately, the doses of 51.2% of SMI medications and 71.4% of sleep medications remained stable across the treatment phase. When considering all medications for a particular participant, 22.8% remained on stable doses of all SMI medications and 68.4% remained on stable doses of all sleep medications across the treatment phase.

The percentage of TranS-C+UC compared to UC-DT participants taking SMI medications was statistically similar at baseline (75.4% vs. 73.3%), post-treatment (73.8% vs. 66.7%), and 6FU (73.8% vs. 66.7%). There was no significant difference in the percentage of participants discontinuing at least one SMI medication at some point during the treatment phase (0% vs. 0%) or during the 6FU (0% vs. 0.03%).

The percentage of TranS-C+UC compared to UC-DT taking sleep medications was statistically similar at baseline (11.5% vs. 15.0%), post-treatment (13.1% vs. 13.3%), and 6FU (16.4% vs. 13.3%). There was no significant difference in the percentage of participants discontinuing at least one sleep medication during the treatment phase (0% vs. 0%) or during the 6FU (0% vs. 0%).

Discussion

Relative to UC-DT, TranS-C was associated with improvement from pre-treatment to post-treatment for all primary outcomes. This confirms our hypothesis that, at post-treatment, TranS-C was superior to UC-DT for functional impairment, general psychiatric symptoms, and sleep and circadian function. These findings were retained at the 6FU for all outcomes except functional impairment, although the means were in the hypothesized direction. These findings replicate prior research showing that sleep treatments improve functioning, symptoms of comorbid mental health conditions as well as sleep and circadian functioning (Geiger-Brown et al., 2015; Taylor & Pruiksma, 2014). In addition, these findings extend prior research by testing a transdiagnostic treatment designed to address a range of sleep and circadian problems experienced by a mixed diagnosis SMI sample in a community setting. CMHC settings are critically important as they treat the most socioeconomically disadvantaged and underserved members of our community, as evident from the demographics in Table 1.

Secondary outcomes were included to index three general psychiatric symptoms: depression, substance use, and hallucinations and delusions. Reduced hallucinations and delusions were observed for TranS-C, relative to UC-DT, from pre-treatment to 6FU. This finding is consistent with prior research showing a tight coupling of psychotic symptoms and sleep (Freeman et al., 2015). However, note that the PSYRATS is only given to those experiencing active psychotic symptoms. Thus, the large effects should be interpreted with caution given the small sample for this analysis. While the total score for depression did not

yield a significant difference between the treatments, an inspection of the means suggests a non-significant advantage on depression for TranS-C. Also, the mean QIDS score for both groups started in the ‘moderate depression range’, which may have limited potential treatment effects. The total score for the measure of alcohol, smoking and substance use also did not yield a significant difference between the treatments. Substance abuse/dependence was exclusionary if it made study participation infeasible. This may have contributed to restricted range. Importantly, the time frame for the ASSIST is the past 3 months or lifetime. At the post-treatment assessment, we assessed the past 2 weeks so the timeframe did not cover the pre-treatment timepoint. Thus, the mean ASSIST score is lower at the post-treatment assessment, relative to the pre-treatment or 6FU assessments; this may have contributed to the null results.

For sleep diary, relative to UC-DT, TranS-C+UC was associated with improved sleep efficiency at all timepoints. Also, relative to UC-DT, TranS-C+UC showed reduced total wake time mean and wake time variability from pre-treatment to post-treatment, and earlier bedtime from pre-treatment to 6FU. There was also a non-significant advantage to TranS-C+UC for total sleep time (which increased by 33 mins from pre-treatment to 6FU, relative to 13 mins for UC-DT) and total wake time (which decreased by 40 mins from pre-treatment to 6FU, relative to 13 mins for UC-DT). For actigraphy, TranS-C+UC showed reduced variability in waking activity count from pre-treatment to 6FU, but no other advantage over UC-DT on other outcomes. Given the problem of the wide transdiagnostic inclusion gates discussed above, we were not surprised that some sleep diary and actigraphy outcomes were not significant. Updated sleep diary and actigraphy reporting standards (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006) may be needed for transdiagnostic samples. There are two other possible contributors to the lack of treatment effects for actigraphy. The GT9X Link does not have an “event marker”, by which a participant indicates going to bed and getting out of bed. Actigraphy itself is not sensitive for these events, which may have reduced validity (Withrow, Roth, Koshorek, & Roehrs, 2019). Also, many participants reported spending substantial periods engaging in motionless behaviors (e.g., watching television), which may have been incorrectly scored as sleep.

For the sleep diary and actigraphy outcomes, it is important to note that these suffer from wide inclusion gates inherent to transdiagnostic research. For example, reducing total sleep time *and* increasing total sleep time can both be treatment goals within TranS-C+UC. Therefore, mean total sleep time does not accurately reflect treatment change. This is also the case for waketime. Within TranS-C+UC, the treatment goal for some participants is to wake earlier (e.g., a patient who sleeps until noon), while for others the goal is to wake later (e.g., a patient who wakes at 4:30am). Again, the mean value will not provide an index of the impact of treatment for a transdiagnostic sample. To address this, we developed a new measure called the Sleep Health Composite (Dong et al., 2019) which combines sleep diary and global indices of sleep for the six sleep health dimensions (see Table 3 in Supplement). On this novel metric, TranS-C+UC exhibited improved sleep health from pre-treatment to post-treatment to 6FU, relative to UC-DT.

As evidenced in Table 1, most participants were diagnosed with insomnia or hypersomnia, whereas only approximately 9.1% of the sample was diagnosed with circadian disturbance.

This estimate is consistent with the prevalence of circadian disturbance for some diagnoses of serious mental illness (e.g., schizophrenia; Reeve et al., 2019) but inconsistent with the prevalence rates of circadian disturbance for other diagnoses (bipolar disorder; Bradley et al., 2017). Of note, in our sample, circadian disturbances were quite common at the subsyndromal level (25.6%). Overall, comorbidity between circadian disturbance and other sleep and circadian disorders was exceptionally common (34.7%) (Sarfani, Hilmoe, Gumpert, Gasperetti, & Harvey, 2020). Together, more research is needed to clarify the prevalence of specific sleep and circadian disorders in patients with psychiatric disorders (Hombali et al., 2019).

Several limitations warrant consideration. We acknowledge that the UC-DT design may inflate the effect size differences (Cunningham, Kypri, & McCambridge, 2013) and that corrections for multiple secondary outcomes were not conducted. The secondary outcomes are not considered confirmatory, replication is needed. Fidelity to the core modules was lower than expected. While there was 100% fidelity to Core Modules 1 and 4, only 68% of cases received Core Module 2 (Daytime impairment) and 58% received Core Module 3 (Unhelpful beliefs about sleep). Due to the severity of impairment present for some individuals, the provider may have focused on the basics of sleep health (i.e., Core Modules 1 and 4). As SMI medications are used to address multiple symptoms including sleep, 13.2% likely under-estimates the use of sleep medications. We had hoped to measure usual care. However, adding to case managers already large and complex workload was not feasible. Assessors were blind to treatment condition, but participants were not. The self-report retrospective primary outcome measures may share method variance. A simplified version of the consensus sleep diary (Carney, 2012) was collected over 7-days as the full version over 14-days was not feasible in the SMI/CMHC context. The inclusion criteria relied on retrospective self-reported estimates of sleep parameters. UC-DT does not control for attention from a therapist. Importantly, while the present study monitored adverse events, adverse events in psychological therapies should be pre-specified, pre-defined and measured (Condon, Maurer, & Kyle, 2020). This is particularly important in sleep treatments as adverse events have been documented (Condon et al., 2020).

In summary, this study adds to the evidence that dysregulated sleep and circadian rhythms in SMI are important and understudied maintaining mechanisms. The findings are consistent with the conceptual model that sleep and circadian dysfunction contribute to vicious cycles of escalating symptoms and dysfunction in SMI (Harvey, 2008). The findings underscore the potential of a transdiagnostic treatment designed to treat a wide range of sleep and circadian problems experienced by adults with a wide range of SMI and support the utility of a novel outcome measure: the Sleep Health Composite. Importantly, this study was conducted in a community mental health setting. This represents a step toward bridging the large gap between research and routine practice. The providers were employed, trained and supervised within a university setting. Hence, it will be important to determine if similar results are obtained by community-based providers. Encouragingly, we compared the demographics of the therapists who delivered the treatment for this study (Gumpert, Yu, Mullin, et al., 2020) with those of a small sample of CMHC providers (Gumpert, Yu, & Harvey, 2020). While the former were younger (Mean age 31 vs. 47), the two groups

were broadly similar for education. Finally, we have discussed our approach to retention and barriers to implementation elsewhere (Gumport, Yu, & Harvey, 2020; Yu et al., 2020).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

Related publications

One manuscript has been published on a subset of participants from the study described in this submission. The focus of the published paper was on different outcomes to those presented in this paper. Thus, there is minimal overlap between the submitted and published papers.

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Public Health Significance.

- This study suggests that the Transdiagnostic Intervention for Sleep and Circadian Dysfunction is an effective treatment for a range of sleep and circadian problems across a range of mental illnesses.
- This study confirms prior research indicating that improving sleep is associated with improvement in mental health symptoms, including psychotic symptoms.

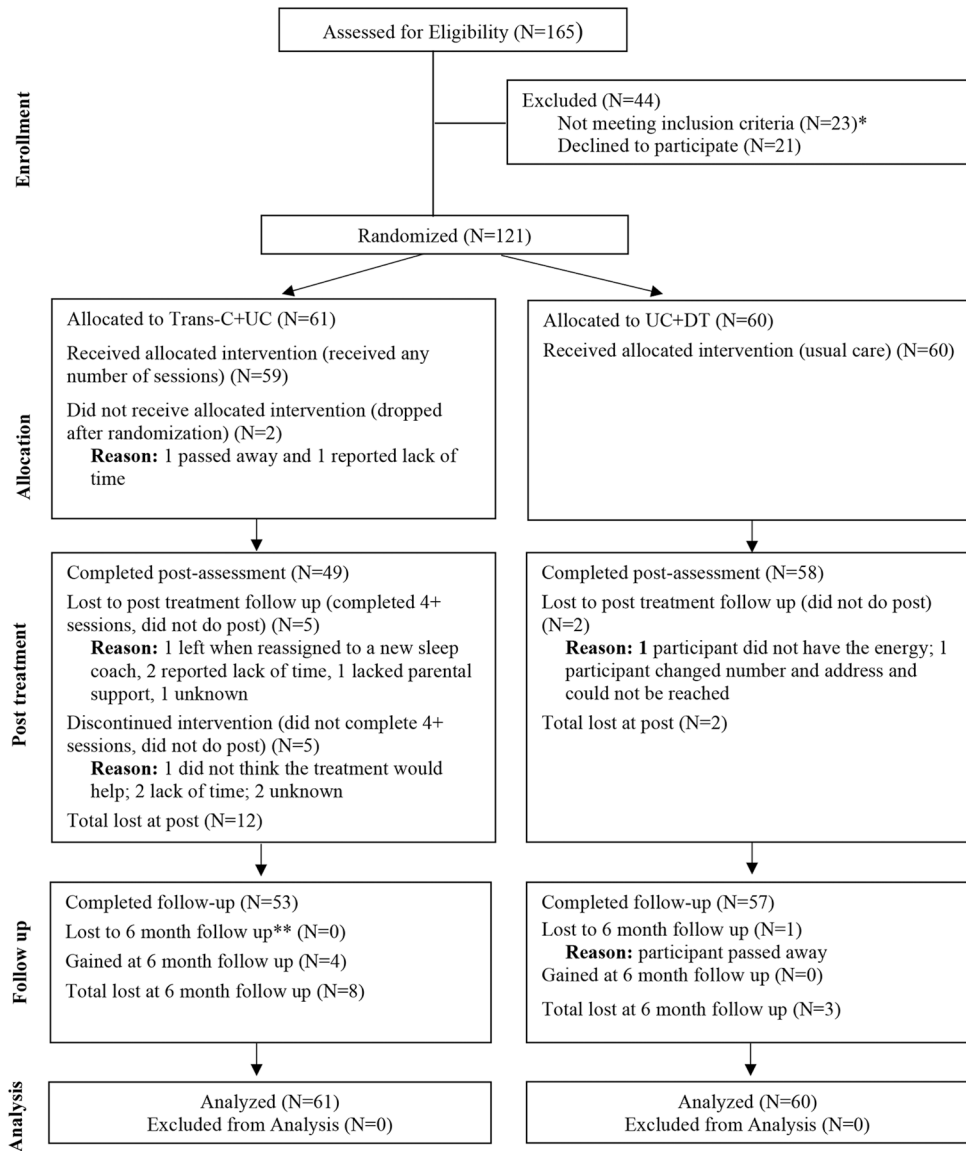
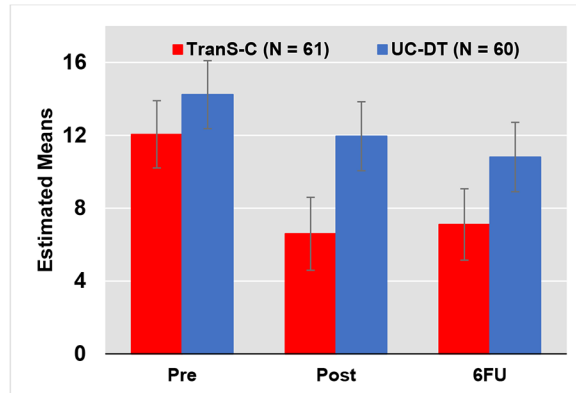


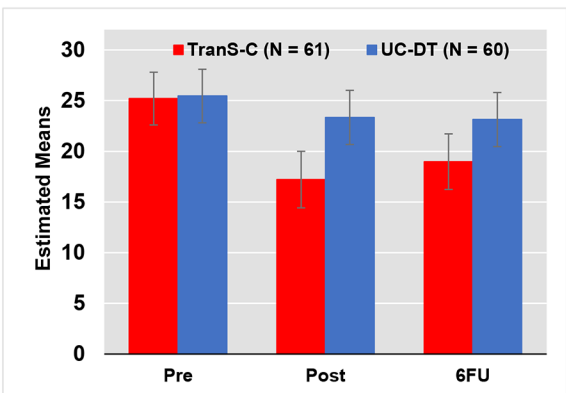
Figure 1. CONSORT Diagram Illustrating the Flow of Participants Through the Study

*Out of 44 who were ineligible, 23 did not meet one of more of the inclusion criteria or met for one or more of the exclusion criteria, and 21 either decided they did not want to participate or stopped contacting the researchers. **6-month follow-up was 6 months from the start of treatment.

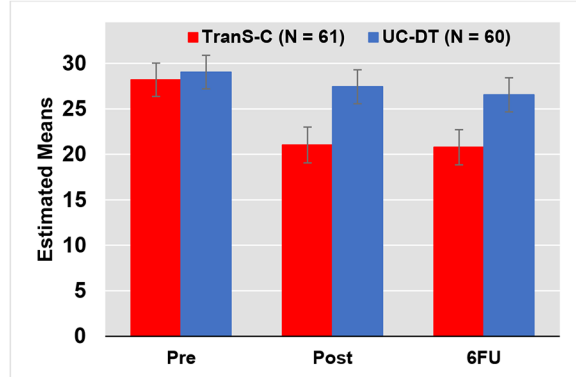
a. Sheehan Disability Scale



b. DSM Cross-Cutting Measure of Symptoms



c. PROMIS-Sleep Disturbance



d. PROMIS-Sleep Related Impairment

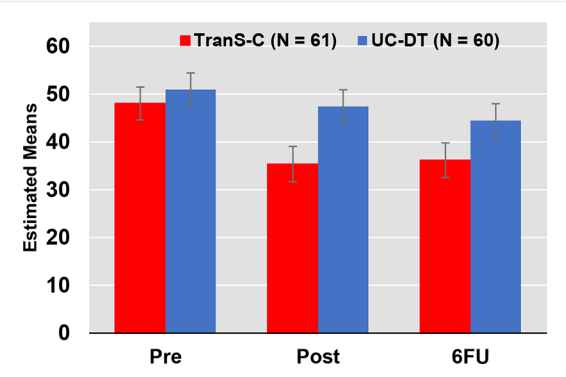


Figure 2.

TransS-C+UC = Transdiagnostic Sleep and Circadian Intervention plus usual care, UC-DT = Usual care and delayed treatment, Pre = Pre-assessment, Post = Post-Assessment, 6FU = 6-month follow-up assessment, PROMIS = Patient-Reported Outcomes Measurement Information System. Error bars indicate 95% CI, plus or minus 2 standard errors.

Table 1.

Baseline Demographic and Clinical Characteristics of Patients in Both Treatment Conditions

Characteristic	UC-DT (n = 60)		Trans-C+UC (n = 61)	
	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			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
Civil status				
Single	42	70.00	38	62.3
Married/common law partner	4	6.67	5	8.2
Separated/divorced/widowed	14	23.33	18	29.51
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			1	1.64
Living arrangement				
Alone	12	20.00	8	13.11
With family (spouse or children)	8	13.33	6	9.84
With friend or roommate or pet	11	18.34	11	18.03
Supported housing ^a	29	48.33	35	57.38
Missing			1	1.64
MINI Diagnosis at pre-treatment (current or past) ^b				
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
DUKE diagnoses at pre-treatment (current) ^b				
Insomnia disorder	49	81.67	52	85.25
Hypersomnolence disorder	14	23.33	17	27.87
Circadian Rhythm Disorder				
Delayed sleep phase type	5	8.33	3	4.92
Advanced sleep phase type	0	0.00	2	3.28
Irregular sleep-wake type	0	0.00	1	1.64
Restless leg syndrome	3	5.00	2	3.28
Periodic limb movement disorder	4	6.67	1	1.64
	M	SD	M	SD
Age (in years)	45.45	13.25	47.97	11.51
Education (in years)	13.38	3.89	13.80	3.05
Annual personal income	\$12,429	\$15,317	\$12,636	\$9,850
Annual household income	\$24,091	\$27,507	\$26,537	\$23,576

Note.

^aSupported housing includes living in board & care homes, senior housing, transitional housing, and homeless shelter. Baseline variables did not differ between treatment conditions.

^bComorbidity was common

Table 2.

Descriptive statistics of outcome variables.

Variable	Pre				Post				FU				<i>d</i> _{pre-post}	<i>d</i> _{pre-FU}		
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>			<i>M</i>	<i>SD</i>
Primary Outcomes																
SDS	14.30	8.51	12.03	6.20	11.76	7.57	6.57	7.07	10.51	8.36	7.00	6.41	7.00	6.41	-0.58	-0.37
DSM5 Cross-Cutting Measure	25.57	10.72	25.05	9.75	23.53	10.59	17.00	11.23	23.07	9.78	18.67	11.38	18.67	11.38	-0.64	-0.42
PROMIS-SD	29.02	6.57	28.26	6.06	27.33	7.22	20.88	8.91	26.40	8.00	20.87	8.50	20.87	8.50	-0.96	-0.82
PROMIS-SRI	51.02	14.09	47.93	11.80	47.22	14.14	35.16	14.01	44.30	15.22	35.65	13.83	35.65	13.83	-0.81	-0.56
Secondary Outcomes																
QIDS	12.50	4.71	12.03	5.15	10.55	5.54	8.88	5.70	10.67	4.58	8.46	5.03	8.46	5.03	-0.20	-0.30
ASSIST	33.68	25.87	39.70	26.68	14.62	17.15	15.35	17.13	32.58	25.25	34.60	24.10	34.60	24.10	-0.18	-0.15
PSYRAIS	36.60	5.13	39.60	14.29	41.73	11.39	36.00	14.82	42.58	9.44	25.80	11.23	25.80	11.23	-1.25	-2.13
WHODAS	81.53	25.56	76.48	21.38	81.48	26.80	68.93	25.53	73.45	26.14	66.63	23.17	66.63	23.17	-0.35	-0.14
Healthy Days Overall Health	3.57	1.17	3.44	1.03	3.40	1.26	3.37	1.27	3.40	1.26	3.37	1.27	3.37	1.27	0.08	0.08
Sleep Diary																
SE mean	77.61	11.89	77.39	13.52	78.93	14.50	84.31	10.07	79.54	12.88	84.78	10.86	84.78	10.86	0.40	0.38
SE variability	12.52	7.63	11.92	6.71	11.86	8.49	10.01	7.95	11.25	6.71	9.24	7.87	9.24	7.87	-0.20	-0.23
TST mean	452.42	101.37	431.06	111.47	459.09	100.16	450.71	92.77	465.23	115.13	464.90	106.54	464.90	106.54	0.11	0.18
TST variability	109.59	55.14	103.96	46.37	123.59	79.11	96.50	97.84	99.30	52.38	90.87	58.77	90.87	58.77	-0.41	-0.10
TWT mean	131.89	80.47	124.84	75.03	131.29	116.57	84.37	49.45	118.92	77.55	83.55	65.53	83.55	65.53	-0.53	-0.39
TWT variability	77.85	54.92	74.04	46.48	82.07	77.64	61.33	62.27	73.27	47.70	52.69	52.56	52.69	52.56	-0.35	-0.38
Bedtime mean	22.20	1.95	22.17	2.36	22.39	1.56	22.00	1.65	22.41	1.88	21.96	2.13	21.96	2.13	-0.17	-0.20
Bedtime variability	1.39	1.06	1.28	0.79	1.41	1.07	1.01	0.93	1.55	1.32	1.00	0.68	1.00	0.68	-0.36	-0.51
Waketime mean	7.90	1.83	7.31	2.02	8.26	2.25	7.31	1.82	7.95	1.83	7.33	1.74	7.33	1.74	-0.20	-0.02
Waketime variability	1.42	0.88	1.34	1.00	1.61	1.11	1.10	1.08	1.22	0.69	1.26	0.95	1.26	0.95	-0.46	0.15
Actigraphy																
TST mean	421.35	126.92	453.65	147.28	411.82	108.28	427.23	135.85	443.24	119.47	437.69	137.88	437.69	137.88	-0.10	-0.28
TST variability	132.08	75.83	132.34	79.71	135.38	75.05	140.06	95.02	144.86	88.72	134.43	96.75	134.43	96.75	0.05	-0.14
TWT mean	91.06	41.52	94.95	55.18	91.39	48.65	90.80	44.85	92.73	41.87	84.51	45.84	84.51	45.84	-0.08	-0.23

Variable	Pre				Post				FU				<i>d</i> pre-FU	
	UC-DT		Trans-C+UC		UC-DT		Trans-C+UC		UC-DT		Trans-C+UC			<i>d</i> pre-post
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD		
TWT variability	55.65	51.16	54.46	48.26	60.36	68.61	51.72	41.86	56.22	48.70	41.41	30.65	-0.15	-0.28
Waking activity count mean	1309.74	532.79	1280.09	607.46	1361.19	532.36	1257.82	680.06	1362.37	598.01	1281.35	667.83	-0.13	-0.10
Waking activity count variability	379.69	211.65	394.04	256.07	393.58	223.01	371.08	310.24	447.29	257.81	354.96	212.71	-0.16	-0.47
Sleep health composite	2.28	1.29	2.54	1.60	2.34	1.33	3.45	1.39	2.53	1.39	3.38	1.64	0.52	0.33

Note. FU = 6-month follow-up. SDS = Sheehan Disability Scale. PROMIS-SD = Patient-Reported Outcomes Measurement Information System–Sleep Disturbance. PROMIS-SRI = Patient-Reported Outcomes Measurement Information System–Sleep-Related Impairment. QIDS = Quick Inventory of Depressive Symptoms. ASSJST = Alcohol, Smoking and Substance Involvement Screening Test. PSYRATS = Psychotic Symptoms Rating Scales. WHODAS = World Health Organization Disability Assessment Schedule 2.0. CDC Healthy Days= overall health question from the 4-question healthy days core module developed by the Centers for Disease Control and Prevention. SE = sleep efficiency (total sleep time/time in bed × 100). TST = total sleep time. TWT = total wake time. BT = bedtime, WT = wake time. *d* pre-post = effect size for treatment effects from pre to post; *d* pre-FU = effect size for treatment effects from pre to 6-month follow-up; both *d*s are calculated using mean change scores and pretreatment raw *SD*s from each treatment condition, based on Feingold equation 5.

Table 3.

Multilevel Modeling Results for Primary and Secondary Outcomes

	Treatment Effect at Baseline			Treatment Effect on Change from Pre to Post			Treatment Effect on Change from Pre to FU6		
	Coef.	SE	P	Coef.	SE	P	Coef.	SE	P
Primary Outcomes									
SDS	-2.18	1.34	0.10	-3.18	1.42	0.025	-1.52	1.40	0.28
DSM5 Cross-Cutting Measure	-0.25	1.89	0.89	-5.88	1.81	0.001	-3.90	1.79	0.03
PROMIS-SD	-0.85	1.33	0.52	-5.55	1.31	<0.0001	-4.92	1.30	<0.0001
PROMIS-SRI	-2.92	2.49	0.24	-9.14	2.44	<0.0001	-5.37	2.42	0.027
Secondary Outcomes									
QIDS	-0.62	0.92	0.50	-0.95	0.95	0.32	-1.67	0.94	0.08
ASSIST	0.26	0.24	0.26	-0.09	0.24	0.72	-0.08	0.23	0.74
PSYRATS	0.87	5.84	0.88	-2.46	7.08	0.73	-17.52	7.54	0.02
WHODAS	-4.87	4.42	0.27	-7.19	4.18	0.09	-1.13	4.16	0.79
CDC Healthy Days: Overall Health	-0.12	0.20	0.55	0.16	0.21	0.46	-0.34	0.21	0.10
<i>Sleep Diary</i>									
SE mean (min)	-0.46	2.35	0.85	5.68	2.67	0.03	5.89	2.64	0.03
SE variability (min)	-0.33	1.45	0.82	-1.45	1.86	0.43	-1.55	1.84	0.40
TST mean (min)	-24.98	19.33	0.20	24.85	20.60	0.23	34.31	20.36	0.09
TST variability (min)	-3.08	12.89	0.81	-19.90	15.23	0.19	-1.76	15.07	0.91
TWT mean (min)	-6.18	15.62	0.69	-39.33	18.83	0.04	-28.56	18.64	0.13
TWT variability (min)	-2.20	11.18	0.84	-17.57	14.11	0.21	-16.05	13.97	0.25
BT mean	0.06	0.36	0.87	-0.55	0.34	0.10	-0.71	0.34	0.04
BT variability	-0.08	0.19	0.68	-0.31	0.25	0.20	-0.45	0.25	0.07
WT mean	-0.57	0.35	0.11	-0.33	0.38	0.39	-0.02	0.38	0.96
WT variability	-0.10	0.18	0.59	-0.39	0.20	0.047	0.20	0.20	0.30
<i>Actigraphy</i>									
TST mean (min)	36.92	23.14	0.11	-12.68	23.42	0.59	-28.33	23.30	0.22
TST variability (min)	0.15	15.44	0.99	4.65	18.72	0.80	-7.57	18.63	0.68
TWT mean (min)	4.16	8.48	0.62	-4.42	10.14	0.66	-13.34	10.09	0.19
TWT variability (min)	-0.005	0.13	0.97	-0.05	0.17	0.77	-0.22	0.17	0.20

	Treatment Effect at Baseline			Treatment Effect on Change from Pre to Post			Treatment Effect on Change from Pre to FU6		
	Coef.	SE	p	Coef.	SE	p	Coef.	SE	p
Waking activity count mean	-41.19	107.66	0.70	-76.85	80.83	0.34	-87.15	79.93	0.28
Waking activity count variability	0.01	0.10	0.95	-0.15	0.11	0.18	-0.27	0.11	0.02
Sleep health composite	0.26	0.26	0.32	0.91	0.30	0.002	0.64	0.30	0.03

Note. SDS = Sheehan Disability Scale, DSM 5 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, QIDS = Quick Inventory of Depressive Symptoms, ASSIST = Alcohol, Smoking and Substance Involvement Screening Test, PSYRATS = Psychotic Symptoms Rating Scales, WHODAS = World Health Organization Disability Assessment Schedule 2.0, CDC Healthy Days: overall health question from the 4-question healthy days core module developed by the Centers for Disease Control and Prevention, SE = sleep efficiency (total sleep time/time in bed × 100), TST = total sleep time, TWT = total wake time, BT = bedtime, WT = wake time. All the *p*-values in bold are the exact *p*-values and remained significant after applying the Benjamini-Hochberg procedure with a 5% false discovery rate assumed.