The Impact of Cognitive Behavioral Therapy for Insomnia on Sleep Log and Actigraphy Outcomes in People with Multiple Sclerosis: A Secondary Analysis

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¹Department of Physical Therapy, Rehabilitation Science, and Athletic Training, University of Kansas Medical Center, Kansas City, KS, USA; ²Sleep Disorders Clinic, Cleveland Clinic, Cleveland, OH, USA **Purpose:** While studies indicate cognitive behavioral therapy for insomnia (CBT-I) improves self-report sleep outcomes from questionnaires in people with multiple sclerosis (MS), it is unclear if CBT-I improves outcomes from a sleep log or sleep assessed objectively via actigraphy in people with MS. This study aimed to determine if CBT-I improves sleep log and actigraphy outcomes in individuals with MS.

Patients and Methods: Twenty-five participants (M_{age} = 53.04, SD= 10.90) were included in this secondary analysis of data from a pilot randomized control study to assess the feasibility and treatment effect of CBT-I in individuals with MS. Participants were asked to maintain a sleep log and wear an actigraph for a week at baseline and post-intervention. Participants were randomized into one of three groups (CBT-I, active control, or one-time brief education control group). One-way ANOVAs were used to assess for group differences and within group change in sleep latency, sleep efficiency (SE), time in bed, total sleep time (TST), wake after sleep onset, variability of SE, and variability of TST.

Results: CBT-I resulted in an increase in sleep efficiency (SE) and decrease in time in bed (TIB) and variability of SE from the sleep log. The CBT-I group also experienced a decrease in TIB and total sleep time (TST) from actigraphy. The active control group demonstrated an increase in variability of SE from actigraphy.

Conclusion: This study indicates that individuals with MS may experience an improvement in sleep log and actigraphy sleep outcomes following CBT-I, but findings need to be replicated in a larger prospective study. The decrease in TST from actigraphy mirrors results from prior studies. **Keywords:** multiple sclerosis, cognitive behavioral therapy for insomnia, sleep log, actigraphy

Introduction

Individuals who undergo cognitive behavioral therapy for insomnia (CBT-I) demonstrate improved self-report sleep measures following the intervention.^{1–4} Questionnaires are often used to assess improvement in sleep outcomes following CBT-I, including improved perception of insomnia severity using the Insomnia Severity Index (ISI) and improved perception of sleep quality using the Pittsburgh Sleep Quality Index (PSQI).^{1,2,4}

A sleep log is another self-report method to determine improvement in sleep outcomes following CBT-I. Wake after sleep onset (WASO), time in bed (TIB), and

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sleep onset latency (SOL) have been shown to decrease and sleep efficiency (SE) and total sleep time (TST) have been shown to increase following CBT-I according to sleep log.^{1,2,5–8} While outcomes from questionnaires are more commonly reports and are perhaps more convenient than sleep logs, a sleep log may be particularly useful because it collects sleep data over multiple nights, often over a week or two.9 However, data from sleep logs are often averaged for the time period the log is kept, so more nuanced outcomes such as sleep patterns and sleep variability are not often considered. 10

Though there is substantial evidence of improvements in self-report sleep measures following CBT-I, there is less evidence regarding the improvement of objectively assessed sleep outcomes. It is important to assess sleep both through self-report questionnaires as well as objective methods because perception of sleep disturbances is often worse than objectively assessed sleep outcomes¹¹ due to anxiety, depression, or other factors. 12,13 A recent metaanalysis reported a statistically significant reduction in SOL and TST (~30 min) assessed using actigraphy following CBT-I and a small nonsignificant change in WASO and SE. 8 The meta-analysis also found no statistically significant improvements in PSG outcomes.8 While PSG is considered the "gold standard" to assess sleep characteristics and stages, a benefit of actigraphy is it assesses sleep outcomes across multiple nights, allowing sleep patterns and variability to be assessed. 14,15 However, actigraphy data are typically averaged over the length of time the sleep data were collected, so information on sleep patterns and variability is seldom reported. No studies to our knowledge have reported if sleep variability assessed by actigraphy improves after CBT-I. Given that sleep regularity is a goal of CBT-I, 16 assessing objectively assessed sleep variability via actigraphy is a current gap in the literature.

Approximately 70% of individuals with multiple sclerosis (MS) experience sleep disturbances, ¹⁷ and at least 40% experience chronic insomnia.¹⁸ Furthermore, sleep disturbances in individuals with MS have been associated with cognitive dysfunction, poorer quality of life, and increased disability, fatigue, depression, and anxiety. 19-23 Thus, an effective intervention to address insomnia in people with MS is paramount. Recent studies have suggested CBT-I improves self-report sleep outcomes in people with multiple sclerosis (MS).²⁴⁻²⁷ A case series studying CBT-I in 11 individuals with MS showed that most participants reported a decrease in overall insomnia (6 of 7), depression (5 of 10),

and fatigue (6 of 10), and an increase of TST (8 of 11).²⁴ Siengsukon et al recently found individuals with MS exhibited significant improvements in insomnia symptoms, sleep quality, fatigue, self-efficacy, and depression symptoms after traditional in-person CBT-I.²⁷ as well as after webbased CBT-I intervention.²⁶ However, it remains unclear if individuals with MS have an improvement in sleep log outcomes or objectively assessed sleep outcomes following CBT-I. Also, it is unknown if CBT-I improves sleep variability in people with MS.

Therefore, the purpose of this secondary analysis is to determine if CBT-I improves sleep outcomes as reported by a sleep log and actigraphy in people with MS. We hypothesized participants would demonstrate significant decreases in SOL, TIB, and WASO and increases in SE and TST following a CBT-I intervention assessed using sleep log and reduction in SOL, TIB, and TST assessed using actigraphy. We also hypothesized that TST and SE would be less variable following CBT-I.

Patients and Methods

The methods of the pilot randomized control study to assess the feasibility and treatment effect of CBT-I to improve sleep quality and fatigue in individuals with MS have been previously reported.²⁷ In brief, participants were recruited from the MS specialty clinic at the University of Kansas Medical Center (KUMC), the National Multiple Sclerosis Society (NMSS), and the KUMC Frontiers Research Participant Registry. Informed consent was obtained from all individuals included in the study. This study was approved by KUMC's Institutional Review Board, and all procedures performed in studies involving human participants were in accordance with the ethical standards of KUMC's institutional review board and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Participants were included in the study if they were between 18-64 years old, had relapsing-remitting or secondary-progressive MS, reported difficulty falling asleep, maintaining sleep or waking up early 3 or more nights per week for at least the last 6 months, scored \geq 10 on the Insomnia Severity Index [ISI]; 7 spoke English, and scored ≥ 24 on the Mini Mental State Exam (MMSE). Participants were excluded if they: had a known untreated sleep disorder, scored > 4 on STOP BANG, scored at increased risk on RLS-Diagnosis Index. scored ≥ 15 on Patient Health Questionnaire [PHQ-9], ²⁸ had a history of alcohol/drug dependence or nervous system disorder other than MS, had a severe neurological or Dovepress Williams-Cooke et al

sensory impairment that would significantly impact testing. had a relapse or used a corticosteroid in the past 8 weeks, or performed shift work. Prior to being randomized into one of three groups (CBT-I, active control [AC], or one-time brief education control [EC]), participants completed a baseline assessment on insomnia severity, fatigue impact, depression, anxiety, and sleep self-efficacy. Participants in the CBT-I group participated in a 45-60-minute standardized weekly program based on a manual by Perlis et al. 16 The AC group participated in weekly 45-60-minute gentle stretching and thinking activities (ie, Sudoku, card games, Wii games), whereas the EC group received one brief session of verbal and written sleep promotion education. Participants were randomized to their groups following baseline assessment, and research personnel responsible for baseline and post-intervention reassessments and scoring of the actigraphy data were blinded to the participants' group assignment.

Sleep Log Data Collection

Participants were asked to maintain a sleep log based on the Consensus Sleep Diary²⁹ for a week at baseline and postintervention (or after 6 weeks for the EC group) while wearing an actigraph (Model wGT3X-BT, ActiGraph Corp, Pensacola, FL, USA) on their non-dominant wrist. Participants were instructed to keep the sleep log in a place where they would remember to fill it out each day (ie, nightstand) and to complete the sleep log daily when they woke up for the day. To complete the sleep log, participants were instructed to estimate the time when they got in bed, attempted to fall asleep, how long it took to fall asleep, time when they woke up, time they got out of bed, how long they lied in bed awake during the night, the amount of time spent out of bed during the night (ie, going to the bathroom), and napping information (eg, nap duration). Participants were also instructed to leave comments to indicate issues that might have affected their sleep pattern (ie, sleeping in a novel environment). TIB was calculated from the time the participant got in bed to the time they got out of bed. TST was calculated by subtracting their SOL, time spent awake out of bed, and time spent lying awake in bed for that night from their TIB. WASO was calculated by summing the amount of time spent awake out of bed and time spent lying in bed awake. To calculate SE for each night, TST was divided by TIB and multiplied by 100. Average SOL, TIB, TST, SE, and WASO was calculated for the week for each participant. Pre- and post-intervention variability scores (also called the coefficient of variance; CV) for SE and TST were

calculated by dividing the participant's weekly SE and TST standard deviation by the weekly SE and TST mean and multiplying by 100, respectively. Intraindividual variability (IIV) has been associated with increased stress, and negative affect, cognitive dysfunction, and insomnia, as well as distinguishing between comorbid symptoms in people with MS. CV is the most common method used to quantifying IIV.

Actigraphy Data Collection

Participants were instructed to wear an actigraph for one week at baseline and post-intervention to collect data on their nightly sleep characteristics (ie, SOL, SE, TIB, TST, WASO). Research personnel fitted an actigraph snuggly, yet comfortably, directly on the skin of the participant's non-dominant wrist at the end of the baseline visit. Actigraphy has been shown to be a valid and reliable method to assess sleep behavior³⁴ and has been used to study sleep outcomes in people with MS. 17,35-37 Participants were instructed to wear the actigraph 24 hours/day during the one week and to remove the actigraph only during periods in which the actigraph would be submerged in water for longer than thirty minutes (ie, swimming, bathing). If any irritation or difficulty wearing the actigraph was experienced, participants were instructed to remove the actigraph and contact the research team. Participants in the EC group were given a postage-paid envelope to return the actigraph after baseline assessment, and all participants returned the actigraph via mail following post-intervention. Participants in the CBT-I and AC group returned the actigraph after baseline assessment at their first CBT-I or AC session, respectively.

Actigraphy data were analyzed by a trained researcher using the Cole–Kripke algorithm within ActiLife software [Version 6.11.9]. ³⁸ Sleep log data were utilized to aid in scoring corresponding actigraphy data. ³⁴ Participant data were included in analysis if they had 10 hours of wear time for at least four valid days. ³⁹

All data were analyzed utilizing IBM SPSS Statistics version 25 (SPSS Inc., Chicago, IL, USA) with alpha set at 0.05. Averages and standard deviations and/or frequency were calculated for demographics. One-way ANOVAs were analyzed for group differences at baseline for age and MS duration. Chi-square analyses were conducted to assess for group differences on gender, race, and type of MS. One-way ANOVAs were used to assess for group differences in sleep latency, SE, TIB, TST, WASO, variability of SE, and

variability of TST for baseline sleep log and actigraphy outcomes. One-way ANOVAs were used to generate parameter estimates to assess the significance of change scores (reassessment score–baseline score) for sleep log and actigraphy outcomes. Effect size (ES; Cohen's d) were used to determine the magnitude of change in the outcome measures from baseline to reassessment for sleep log and actigraph outcomes. Cohen's d was interpreted as small d=0.2, medium d=0.5, and large d=0.8, respectively.⁴⁰

Results

Overall, there were 30 participants in the parent study. However, only 25 participants (eight individuals in the CBT-I group, nine in the EC group, and eight in the AC group; Table 1) were included in this secondary analysis due to missing actigraphy data at baseline and/or reassessment. There were no group differences (Table 1) on gender, race, age, MS type, or MS duration. There were no significant differences between the groups at baseline for the sleep log and actigraphy outcomes (p > 0.05).

For the sleep log outcomes (Table 2), the CBT-I group showed a significant increase in SE (p = 0.006, ES = 1.203) and reduction in TIB (p = 0.001, ES = 0.993) and variability in SE (p = 0.026, ES = 0.657) from baseline to post-intervention, but no change in the other sleep log variables. The EC and AC groups did not show a significant change from baseline to post-intervention for any of the sleep log outcomes.

For the actigraphy outcomes (Table 3), the CBT-I group demonstrated a significant reduction in TIB (p = 0.005, ES = 0.925) and TST (p = 0.004, ES = 0.893) from baseline to post-intervention. The active control group showed a significant increase in variability in SE (p = 0.004).

0.035, ES = 0.463). There were no significant changes for the other actigraphy variables.

Discussion

This is the first study to examine if CBT-I improves sleep outcomes assessed with sleep log and actigraphy in people with MS. Only the CBT-I group demonstrated an improvement in sleep outcomes on the sleep log and a reduction in TIB assessed using actigraphy and sleep log. Using actigraphy, the CBT-I group also showed a decrease in TST and the AC group demonstrated an increase in SE variability. These results suggest that CBT-I has a positive effect on self-report sleep log and objectively assessed sleep outcomes in people with MS.

Our findings of increased SE and decreased TIB as reported by a sleep log following CBT-I supports the findings of previous research. A recent meta-analysis reported an average 9% increase in sleep log SE following CBT-I. Participants in the current study demonstrated a 16.20% increase in sleep log SE following CBT-I. Also, participants in the current study demonstrated a 60.79-minute decrease in TIB following CBT-I, which supports results from prior CBT-I and sleep restriction therapy studies. 5,41,42 However, our study did not find a significant reduction in SOL or WASO or a significant increase in TST which has been reported in prior metaanalyses. 1,2,8 This may be due to the small sample size or the comorbid issues that are often experienced by individuals with MS (ie, pain, spasticity, fatigue) that may impact the improvement in these other sleep outcomes.

The results of our study also support findings from a meta-analysis⁸ that TST assessed by actigraphy decreases initially following CBT-I. Sleep restriction

Table I Participant Demographics by Group

	CBT-I (n = 8)	Brief Education (n = 9)	Active Control (n = 8)	p-value
Gender	I Male 7 Female	9 Female	I Male 7 Female	0.543
Race	7 White I Black	9 White	8 White	0.543
Age (years)	49.25 (7.72)	58.78 (8.66)	50.38 (13.96)	0.139
Multiple Sclerosis Type	7 RR I SP	8 RR I SP	8 RR	0.596
Disease Duration (years)	13.88 (5.14)	19.22 (11.72)	8.88 (10.02)	0.104

Notes: Gender, Race, and MS Type reported as n; Age and Disease Duration reported as mean (standard deviation). **Abbreviations:** RR, remitting–relapsing; SP, secondary progressive.

Table 2 Descriptive Statistics of Sleep Log Data by Group

CBT·I (n = 8)						Brief Education $(n = 9)$	ion (n = 9)				Active Control (n= 8)	rol (n= 8)			
	Pre-	Post-	Change	d	ES	Pre-	Post-	Change	d	ES	Pre-	Post-	Change	ф	ES
Latency (min)	24.59 (24.70)	10.82 (7.12)	-13.76 (20.46)	0.130	0.673	26.48 (13.67)	15.43 (7.26)	-11.05 (14.54)	0.136	0.760	22.45 (19.30)	18.37 (19.63)	-4.07 (28.33)	819:0	0.144
(%) SE	75.17 (9.19)	87.34 (7.56)	12.17 (10.12)	900.0	1.203	75.79 (10.72)	78.21 (16.35)	2.41 (10.90)	0.457	0.222	76.21 (13.42)	77.08 (12.91)	0.86 (6.65)	0.813	0.132
TIB (min)	560.85 (90.41)	479.88 (59.43)	-80.97 (81.50)	0.001	0.993	504.53 (88.10)	489.30 (110.28)	-15.22 (41.36)	0.386	0.368	522.68 (103.06)	505.35 (109.59)	-17.32 (23.85)	0.84	0.731
TST (min)	417.64 (58.30)	416.90 (43.02)	-0.73 (47.88)	0.973	0.015	391.01 (108.46)	386.90 (132.06)	-4.10 (53.75)	0.817	0.077	393.74 (87.10)	385.06 (76.77)	-8.68 (54.16)	999:0	0.160
WASO (min)	25.15 (6.03)	31.65 (13.48)	6.50 (18.82)	0.481	0.345	21.27 (9.83)	32.27 (21.00)	10.99 (22.68)	0.153	0.485	26.38 (22.70)	32.54 (19.01)	5.58 (23.98)	0.513	0.251
VariSE (%)	20.81 (12.62)	10.63 (7.06)	-10.18 (15.47)	0.026	0.657	16.25 (10.57)	11.65 (6.73)	-4.59 (8.23)	0.199	0.559	14.37 (8.92)	14.89 (9.69)	0.51 (7.04)	968:0	0.074
VariTST (%)	27.38 (18.33)	15.44 (8.59)	-11.94 (22.52)	0.130	0.530	33.08 (17.84)	25.80 (19.52)	-7.27 (20.16)	0.252	0.361	17.01 (8.61)	23.78 (10.93)	6.77 (10.80)	0.344	0.627
		7													

Note: Data reported as mean (standard deviation).

Abbreviations: SE, sleep efficiency; TIB, time in bed; TST, total sleep time: WASO, wake after sleep onset; VariSE, variability of sleep efficiency; VariTST, variability of total sleep time.

Table 3 Descriptive Statistics of Actigraphy Data by Group

CBT: (n = 8)	8)					Brief Education $(n = 9)$	tion (n = 9)				Active Control (n = 8)	rol (n = 8)			
	Pre-	Post-	Change	d	ES	Pre-	Post-	Change	d	ES	Pre-	Post-	Change	р	ES
Latency (min)	3.71 (3.05)	2.46 (2.35)	-1.24 (4.30)	0.413	0.291	5.38 (5.49)	4.21 (3.01)	-1.16 (4.78)	0.417	0.244	3.69 (3.33)	2.90 (1.44)	-0.79 (3.38)	109.0	0.234
SE (%)	89.41 (5.24)	89.51 (4.67)	0.09 (3.27)	0.971	0.031	87.47 (5.54)	85.40 (10.99)	-2.07 (11.12)	0.421	0.186	87.98 (7.63)	88.99 (4.66)	1.01 (5.34)	0.708	0.189
TIB (min)	513.14 (84.01)	452.35 (43.09)	-60.79 (65.78)	0.005	0.925	506.81 (69.85)	489.00 (87.12)	-17.81 (55.61)	0.346	0.320	541.73 (124.88)	502.97 (106.47)	-38.75 (42.36)	0.061	0.913
TST (min)	458.35 (82.56)	406.18 (49.55)	-52.17 (58.39)	0.004	0.893	443.57 (71.58)	436.75 (95.66)	-6.81 (47.31)	0.665	0.144	470.88 (91.27)	446.58 (87.84)	-24.30 (29.35)	0.155	0.828
WASO (min)	51.07 (28.02)	44.82 (17.09)	-6.24 (23.69)	0.550	0.264	57.85 (29.34)	48.02 (29.95)	-19.16 (27.66)	0.061	0.513	63.40 (49.34)	53.48 (32.55)	-9.91 (34.97)	0.345	0.269
VariSE (%)	5.91 (3.52)	4.30 (2.39)	-1.60 (2.01)	0.794	0.800	8.40 (5.66)	8.55 (8.13)	0.15 (7.01)	0.979	0.021	6.36 (3.53)	20.01 (27.75)	13.65 (29.53)	0.035	0.463
VariTST (%)	14.21 (2.60)	14.38 (4.06)	0.16 (4.67)	0.970	0.050	26.85 (18.48)	19.93 (9.04)	-6.91 (18.66)	0.109	0.371	14.76 (3.63)	19.76 (6.39)	4.99 (8.04)	0.267	0.623

Note: Data reported as mean (standard deviation).

Abbreviations: SE, sleep efficiency; TIB, time in bed; TST, total sleep time; WASO, wake after sleep onset; NOA, number of awakenings; AwkLnght, awakening length; VariSE, variability of sleep efficiency; VariTST, variability of total sleep time.

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therapy (SRT) and stimulus control are components of CBT-I to increase sleep drive and reduce negative associations with the bed, but these techniques may lead to a temporary initial reduction in TST. 16,43 This temporary initial reduction in TST may not be perceived by the individual (as evidenced by lack of reduction of TST reported on the sleep log) if their sleep quality has improved or if their expectation is for an increase in TST. Given this, it may be that the CBT-I group of our study was still adjusting to the skills learned in CBT-I, and that TST would have improved if reassessed further out from completion of the intervention. Another possible explanation for the reduction in TST is that actigraphy can misclassify quiet, non-movement awake lying in bed as sleep rather than wake, so the reduction in TST could be due to the participants spending less time in bed. The latter explanation seems more plausible as there were no other deleterious outcomes for this group, and the CBT-I group reported an increase in TST on their sleep log. In fact, the CBT-I group demonstrated significant improvements in insomnia severity, sleep quality, sleep self-efficacy, and other health-related outcomes including depression and fatigue, which would suggest a positive overall impact of CBT-I on the participants.²⁷ Furthermore, many studies failed to find actigraphy differences following CBT-I in small sample sizes, perhaps indicating that CBT-I may be even more impactful in those with MS than some other populations.

Our result that CBT-I decreases SE variability supports prior studies that report reduced variability of sleep outcomes following in-person 44,45 and internet-delivered CBT-I⁴⁶ and Brief Behavioral Therapy (BBT-I).⁴⁷ One might expect that CBT-I would yield a decrease in the variability of SE given a regular wake up time and time to bed is encouraged within the context of stimulus control therapy, SRT, and sleep promotion education. Sleep variability is an important albeit seldom used outcome as it demonstrates how sleep can change from night to night versus the mean of several nights of data which excludes variability information. 15 For example, an individual could have SE of 75% for night one, 95% on night two, and an SE of 55% on night three. Had we simply averaged these nights of data, which is what is typically done, we would report an overall SE of 75% and missed the interesting insight contained in examining variability. Another individual could have SE of 75% for all three nights, which would have also yielded a mean SE of 75% but with no variability. Also, considering sleep variability is

important as previous research has demonstrated that sleep variability is associated with symptoms of insomnia, increased stress, reduced cognitive functioning, negative affect, diabetes, and heart conditions. Thus, it is important that sleep is examined in multiple ways (ie, duration, quality, variability) to gain a better understanding of how CBT-I, or other interventions, affect sleep and related health outcomes.

The discrepancy between the findings on the sleep log and actigraphy is not surprising as it is well documented that self-report and objective data are different constructs. Selfreport sleep measures assess one's beliefs and perceptions about sleep, whereas objective sleep measures (ie, actigraphy) assess sleep/wake behaviors. 48 Adults often perceive and report their sleep disturbances to be more severe than measured by objective measures, 11 which may be due to anxiety, depression, or other factors. 12,13 Another issue with sleep logs is that participants are asked to estimate the time (not watch the clock) and to remember that estimate the next morning to complete the sleep log. Estimating time is difficult for some individuals as is recalling information the following morning. 49,50 Furthermore, self-report outcomes can be influenced by expectations of improvement as a result of participating in an intervention study whereas actigraphy would not be impacted by expectations.⁵¹ However, objective sleep measures may also not be sensitive enough to the changes experienced by those practicing CBT-I, whereas self-report measures are. 52 Other objective sleep measures such as circadian biomarkers, sleep fragmentation, and sleep architecture may aid in further understanding the changes demonstrated in participants following CBT-I.⁵²

There are limitations of this study. There was a small number of participants in each group, which limits the interpretation of the results, and multiple ANOVAs were run on the same sample increasing the type 1 error. Also, this study consisted predominately of white females, which limits the generalizability of these findings. While females are 2-3 times more likely to develop MS than men,⁵³ a recent study also reports that African Americans have an increased risk of developing MS compared to Whites. 54,55 Also, this study was a secondary analysis. and the outcomes examined in this work were not the primary outcomes of the original study. In addition, though actigraphy is a valid measure of sleep compared to PSG³⁴ and has been used to study sleep outcomes in people with MS, 17,35-37 currently used algorithms may not take into account symptoms (ie, tremors, muscle spasms, muscle paralysis) often experienced by individuals with MS.³⁴

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Conclusion

In sum, this study demonstrated that CBT-I can improve sleep outcomes via sleep log and actigraphy in people with MS. This study further illustrates the importance of including both self-report sleep outcomes and objective outcomes as they are separate albeit important constructs. This study also encourages researchers and clinicians to consider sleep variability as a vital outcome to consider in research studies and the clinical setting.

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Disclosure

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