JCSM | Journal of Clinical Sleep Medicine

The *Journal of Clinical Sleep Medicine* is dedicated to advancing the science of clinical sleep medicine. In order to provide subscribers with access to new scientific developments as early as possible, papers are posted prior to their final publication in an issue.

These papers undergo minor formatting for readability but are otherwise posted as accepted—without copyediting or final formatting by the publisher. In some instances, substantial changes are made during the copyediting and formatting processes; therefore, the final version of the paper may differ significantly from this version.

Media & Public Relations: Embargo Policy

A submitted paper is embargoed until it is posted as an "accepted paper" on the journal website. At that time, the paper is no longer embargoed and may be promoted before its final publication in an issue. Although the full text of an accepted paper is available to subscribers only, the abstract is available to the public. The DOI number is a permanent identifier for the article, and the DOI link below should be used in a press release to link to the study. Please contact the public relations department of the American Academy of Sleep Medicine with any questions at media@aasm.org or 630-737-9700.

https://doi.org/10.5664/jcsm.10572

Randomized controlled trial of cognitive behavioral therapy for perinatal insomnia: postpartum outcomes

Running Title: Postpartum outcome of CBT for insomnia

Rachel Manber, PhD[1]; Bei Bei, DPsych(Clinical), PhD[2]; Sooyeon Suh, PhD, DBSM[1,3]; Norah Simpson, PhD[1]; Elizabeth Rangel, BA[1]; Anita Sit, MD[4]; Deirdre J. Lyell, MD[5]

[1]*Stanford University School of Medicine, Department of Psychiatry and Behavioral Sciences*
[2]*Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University*
[3]*Sungshin Women's University, Department of Psychology*
[4]*Santa Clara Valley Medical Center, General Gynecology and Obstetrics Division*
[5]*Stanford University School of Medicine, Department of Obstetrics and Gynecology*

Address correspondence to: Sooyeon Suh, PhD, DBSM, Department of Psychology, Sungshin University, Seongbuk-gu Bomunr-ro 34 da-gil 2, Seoul, Korea 02844; Tel: +82-2-920-7215; Email: alysuh@sungshin.ac.kr

DISCLOSURE STATEMENT

Funding: NIH R01 NR013662. The authors report no conflicts of interest.

Number of tables: 3
Number of figures: 2
Manuscript word Count: 4588

ABSTRACT

Study Objectives: This study aimed to assess the effectiveness of cognitive behavioral therapy for insomnia (CBTI) during the postpartum period, as part of a larger randomized controlled trial of CBTI on perinatal insomnia.

Methods: 179 women of 18 to 30 gestational weeks with insomnia disorder were randomized to CBTI or an active control (CTRL) therapy. Participants were assessed between 18-32 weeks of pregnancy at baseline, after the intervention during pregnancy, and at 8, 18, and 30 weeks postpartum. The primary outcome were the Insomnia Severity Index (ISI) and total awake time (TWT), defined as minutes awake during the sleep opportunity period, assessed with actigraphy and sleep diaries. Included in the analyses were women who provided data for at least one of three postpartum assessments (68 in CBTI; 61 in CTRL).

Results: Piecewise mixed-effects models revealed a main effect reflecting reduction in ISI scores from 8 to 18 weeks postpartum ($p = .036$) and a non-significant increase from 18 to 30 weeks; significant effects for group allocation were present only in week 30 ($p = .042$). CTRL participants reported significantly longer time awake, excluding time spent caring for the infant, at each postpartum assessment; time awake at night caring for the infant did not differ between groups. There was no significant group difference in the postpartum trajectory of actigraphy measured TWT, the two diary measures of time awake (p-values $> .05$). CBTI participants with at least 50% reduction in ISI during pregnancy had consistently stable ISI scores (mean < 6) during the postpartum period; those in CTRL had variable ISI scores over time with large individual differences.

Conclusions: For women with insomnia disorder during pregnancy, CBTI initiated during pregnancy conferred postpartum benefits in terms of wakefulness after sleep onset (excluding time spent caring for the infant) and insomnia severity, though the latter emerged only later in the postpartum period. These findings underscore the importance of treating insomnia during pregnancy, a conclusion that is further supported by our finding that pregnant women who responded to insomnia treatment during pregnancy experienced better sleep in the postpartum period.

Clinical Trial Registration: Clinicaltrials.gov, NCT01846585

Keywords: insomnia; pregnancy; postpartum; CBTI

BRIEF SUMMARY

Current Knowledge/Study Rationale: Women during pregnancy were randomized to cognitive behavioral therapy for insomnia (CBTI) or a control therapy for insomnia. The current study assessed the effectiveness of CBTI provided during pregnancy on sleep during the first 30 weeks postpartum.

Study Impact: Using data from all women who provided data at one or more postpartum assessments (68 in CBTI; 61 in CTRL), we found that CBTI was associated with less time awake at night that was not due to infant care at 8, 18, and 30 weeks postpartum and lower insomnia severity at 30 weeks postpartum. We also found that women with at least a 50% reduction in ISI scores during pregnancy had lower insomnia severity during the postpartum period. It appears that CBTI initiated during pregnancy confers benefits for postpartum sleep, a time when being awake to care for infants at night is inevitable and that later in the postpartum period, when needs for nocturnal infant care tend to decrease, the benefits also include lower insomnia severity. Our findings underscore the importance of treating insomnia during pregnancy, a conclusion that is further supported by our finding that pregnant women with insomnia who had lower insomnia symptoms following insomnia treatment experienced better sleep in the postpartum period.

INTRODUCTION

Poor sleep is common during pregnancy.[1] Approximately 50-73% of women report insomnia symptoms, with 16-19.8% scoring above threshold for insomnia disorder and are classified as having probable insomnia disorder.[2-5] Approximately 50% of women who endorse probable insomnia during pregnancy continue to have symptoms at two years postpartum.[4] Poor maternal sleep during the postpartum period is associated with a number of negative health outcomes, including increased risk for accidents and elevated depressive and anxiety symptoms.[6-12]

Cognitive behavioral therapy for insomnia (CBTI) is well suited during pregnancy and the postpartum period because it does not require taking sleep medications. Three randomized controlled studies have documented the efficacy of CBTI during pregnancy, including one study where CBTI was delivered by a therapist and the control condition was a credible control therapy of equal duration and two other studies where CBTI was delivered digitally with the control condition being sleep education or treatment as usual for pregnant women with elevated insomnia symptom severity.[13-15] Less is known about the effects of perinatal CBTI on insomnia during the postpartum period among women who had insomnia disorder during pregnancy. A few studies have reported on the effects of prenatal CBTI on postpartum outcomes. Kalmbach et al. (2022) found that, six weeks after childbirth, participants assigned to CBTI reported longer sleep duration and fewer sleep maintenance issues compared to those assigned to the control arm.[16] Felder et al. (2022), who tracked individuals longer-term, found that those who received digital CBTI had higher rates of insomnia remission and lower rates of insomnia cases 6 months after childbirth.[17] Combined, these studies suggest long-term benefits of CBTI on postpartum sleep.

The aim of the current study was to assess the effectiveness of a six-session therapist-delivered CBTI, started during pregnancy, on insomnia severity during the postpartum period. Participants were randomized to CBTI or a control insomnia therapy (CTRL) delivered by therapists at equal frequency and duration. Five sessions were delivered during pregnancy and the sixth at around six weeks postpartum. We previously reported on outcomes during pregnancy.[13] In this study we focus on outcomes during the postpartum period. We hypothesized that, compared to those assigned to CTRL, participants in the CBTI condition would have (a) lower scores on the Insomnia Severity Index (ISI; primary outcome), (b) lower total wake time (TWT), defined as minutes awake during the sleep opportunity period, assessed daily using actigraphy and sleep diary, and (c) on postpartum depression symptom severity, evaluated with the Edinburgh Postnatal Depression Scale (EPDS). We also explored effects on time awake excluding time caring for the infant and whether changes in insomnia symptoms during pregnancy moderated postpartum insomnia outcome.

METHODS

Design

Participants were recruited between May 2013 and April 2017 from a university-based obstetric clinic (Stanford University) and a county-hospital-based (Santa-Clara Valley Medical Center) obstetric clinic and through community advertising. The protocol was approved by Institutional Review Boards at Stanford University and Santa-Clara Valley Medical Center and all participants provided signed informed consent. Participants were randomized with equal probability to receive CBTI or CTRL treatments, delivered by therapists with equivalent credentials and training, at equal frequency and duration. Eligible participants provided pre-treatment data (baseline), including questionnaires, actigraphy and daily sleep diaries. During the pregnancy portion of the study, participants received five weekly treatment sessions, wore actigraphy, and completed the ISI and EPDS weekly and sleep diaries daily. (The results of the primary aim of the study evaluating the effectiveness of the pregnancy portion of treatment after these five sessions was previously reported.[13]) At around six weeks postpartum an additional therapy session was provided. Participants were then assessed at 8, 18, and 30 weeks postpartum using actigraphy, ISI, and sleep diaries.

Participants

The eligibility criteria and screening process have been previously described.[13] Briefly, participants were included if they were speaking English or Spanish, were between 18-32 weeks gestation at the screening visit and met Diagnostic and Statistical Manual for Mental Disorder – Fifth Edition (DSM-5) criteria for insomnia disorder[18]; similar to Kalmbach and colleagues, we modified the minimal duration from three months to one month.[2] Participants were excluded if they had an unstable medical condition, or had prior diagnosis or had clinical symptoms of obstructive sleep apnea (based on a structured clinical interview), Restless Legs Syndrome (RLS) occurring three or more times/week, with an onset prior to pregnancy, severe circadian rhythm sleep-wake disorders; or parasomnias occurring more than once a week.[19] They were also excluded if they had major depressive disorder, panic disorder with nocturnal panic attacks, post-traumatic stress disorder, substance abuse/dependence disorders, bipolar disorder or thought disorders. Participants were also excluded if they were currently receiving any treatment for insomnia or had previously received CBTI. In this study, participants consisted of those who provided data on the ISI, actigraphy, or sleep diary at least at one of the three postpartum assessment timepoints.

Randomization and blinding

Separate randomization lists were generated for each of three recruitment sources. The randomization was performed using blocked randomization with random block sizes of 2, 4, and 6.[20] For additional details see Manber et al. (2018).[13] When a participant became eligible, the treatment coordinator (co-author NS) assigned a participant to a therapist and coordinated scheduling of the first session. To keep the research team masked to treatment condition, the treatment coordinator served as the interface between the research team and the therapists and participants were instructed to not discuss their therapy with the study coordinator. The treatment providers were masked to study hypotheses. They were told the research aims were to investigate two behavioral interventions for insomnia.

Treatments

Both treatment conditions (CBTI and CTRL) consisted of five individual therapy sessions provided in English or Spanish, based on each participant's preference. Details about each therapy, therapists, training, competency and fidelity were previously published by Manber and colleagues (2019).[13] Briefly, CBTI included general education about sleep and sleep during pregnancy and postpartum periods, as well as information about healthy sleep habits. The intervention also included stimulus control, modified to recommend safety naps when experiencing significant daytime sleepiness, as well as time in bed restriction, a modification of the standard sleep restriction therapy,[21, 22] whereby the initial time in bed (TIB) recommendations were equal to average total sleep time (TST) plus 30 minutes (and never less than 5.5 hours). To promote safety, participants were advised to contact their therapist if significant daytime sleepiness emerged, at which point the TIB window was extended, if needed, and safety naps were re-emphasized. The intervention also included cognitive therapy to address sleep interfering thoughts as needed,[21] strategies for reducing cognitive and somatic hyperarousal; and relapse prevention. Mothers were also given guidelines on how to adjust their TIB windows, which during the postpartum period, was further expanded by adding last week's average time spent caring for the infant during the mother's sleep period. The CBTI intervention also included information about infant sleep development and tips for setting the stage for optimal infant sleep development, adapted from Tips for Improving Postpartum Sleep.[23] CTRL therapy was a modified pseudo-desensitization therapy for insomnia, which has been previously and successfully used as a control treatment in RCTs of CBTI.[24-26] It consists of creating a hierarchy of sleep-related distressing situations and a list of neutral situations and a series of desensitization exercises pairing distressing hierarchy situations with the neutral ones. CTRL therapy also included information about sleep, sleep during pregnancy, healthy sleep habits (but not sleep restriction or stimulus control recommendations), infant sleep development and the infant sleep recommendations based on the American College of Pediatrics' recommendations concerning infant sleep that were available in 2013 (Available upon request from the corresponding author upon request.).

Measures

Diagnostic screening measures included the Duke Structured Interview for Sleep Disorders and the MINI International Neuropsychiatric Schedule,[19, 27] The primary outcome was the Insomnia Severity Index (ISI), where, in the general population, scores 14 or more are interpreted as clinically meaningful insomnia and scores below 8 as no insomnia.[28, 29] Secondary sleep outcomes included total wake time (TWT), defined as minutes awake during the sleep opportunity period. TWT was derived from actigraphy (Actiwatch™ ACT2) and separately, as described below, from the Consensus Sleep Diary[30]; both were collected during pregnancy and for a week at each of the three postpartum assessment time points. The Consensus Sleep Diary items related to wake time were adapted to the postpartum period by asking participants to report separately on (a) duration of spontaneous awakenings not related to the infant, (b) time awake caring for the infant, and (c) time awake after caring for the infant. Because, during the early postpartum period, caring for the infant contributes to maternal wakefulness after sleep onset, we calculated, and separately analyzed, two wakefulness variables: time awake to care for the infant (TWT_{infant} ;c above) and time awake excluding time caring for infant (TWT_{other}), defined as the sum of (a) and (b) above plus latency to sleep onset. Participants also completed the Edinburgh Postnatal Depression Scale (EPDS) weekly.[20]

Analysis

Data were analyzed in R 4.1.2.[31] Statistical significance was determined by two-tailed 5% significance level. Effect sizes for continuous variables were quantified using Cohen's *d*, with values above 0.2, 0.5, and 0.8 suggesting small, moderate, and large effect sizes, respectively.[32] In all analyses, discrete time points were used, with daily actigraphy and sleep diary values averaged for each time point before analyses.

To examine group differences in postpartum insomnia levels and trajectories, we carried out a linear mixed effects model with auto-regressive error structure using ISI scores as the outcome. The model included two slopes: Slope 1 represented changes from 8 to 18 weeks postpartum time point, and Slope 2 represented changes from 18 to 30 weeks postpartum time point. Group allocation, recruitment site, and their interactions with Slope 1 and Slope 2 were included as fixed effects while controlling for ISI scores at baseline.[33] The same analysis was carried out for actigraphy measured TWT (respective baseline average values included as covariates), for the two diary reported wakefulness indices, TWT_{infant} and TWT_{other}, and for EPDS (excluding the sleep item). For parsimony, recruitment site and its interactions were dropped in all final models as model comparisons showed non-significant changes to model fit with or without them (all p-values > .05). Extreme values and multivariate outliers were assessed using sensitivity analyses; as a result, five influential data points from three individuals were removed from models related to diary assessed wakefulness; all other models included all available data.

To explore whether change in insomnia severity following pregnancy treatment moderated the trajectory of insomnia severity during postpartum, we added to the above mentioned linear mixed effects model the change scores of the ISI from baseline (at enrollment) to end of pregnancy treatment (after Session 5). Significant three-way interactions amongst Slopes, Group, and ISI pregnancy change scores were visualized, drawing the trajectory of postpartum ISI separately for those with at least 50% reduction in pregnancy ISI relative to those with lesser change in ISI during pregnancy.

RESULTS

Sample characteristics

Of the 254 participants who completed screening, 179 were eligible and provided baseline data. The analyzable sample for this manuscript consists of 129 women who provided data at least at one of the three postpartum time points (n=105 for 8 weeks, n=94 for 18 weeks, and n=102 for 30 weeks). These included 68 who received CBTI and 61 who received CTRL treatment. See **Figure 1** for participant flow

and **Table 1** for baseline characteristics of the participants in the analyzable sample, organized by study arm.

Compared to those who did not provide postpartum data, participants in the analyzable sample for this study were more likely to be White (56.6% vs 26.0%, $p < .001$), less likely to have household income < $55k (70.0% vs 45.5%, $p = .004$), and had significantly lower ISI score after final pregnancy treatment session (M ± SD: 8.96 ± 5.04 vs 12.69 ± 5.44, $p < .001$, $d = 0.73$); all other measures were not significantly different between those provided postpartum data versus those did not, including treatment group allocation (**Table S1** in the supplemental material; p-values > .057).

On average, participants in the analyzable sample received 4.85 (SD = .626) sessions during pregnancy (CBTI participants received 4.91 [SD = .375] sessions and CTRL participants received 4.78 [SD = .818] sessions) and 93% received a postpartum session (91.8% in CBTI and 94.1% in CTRL).

Intervention effects at postpartum

Means and standard deviations of ISI scores and sleep parameters by assessment point and between group differences are presented in **Table 2**. Compared to participants in the CBTI group, those in the CTRL group reported significantly longer TWT_{other} (i.e., wakefulness excluding time caring for infant) at 8, 18, and 30 weeks postpartum.

Results of mixed effects models for ISI are summarized in **Table 3**. For the ISI, the primary outcome, there were no significant group allocation effects, either for the main effect ($p = .677$) or its interaction with the two slopes (p-values > .05). There was an overall reduction in ISI scores from 8 to 18 weeks postpartum ($p = .036$), but changes from 18 to 30 weeks were non-significant ($p = .183$). Higher baseline ISI scores were associated with significantly higher postpartum ISI scores ($p = .002$). Secondary mixed effects models for EPDS revealed no main effects for group, time, or interaction effects ($p > .12$).

Similar to the ISI scores, the two groups also did not differ significantly on postpartum trajectories of actigraphy (p-values > .05 for both main and interaction effects of Group). Actigraphy measured TWT decreased by an average of 30 minutes from 8 to 18 weeks postpartum ($p < .001$) and then increased by an average of about 10 minutes from 18 to 30 weeks ($p = .041$). Examining group differences at each time point revealed little differences at 8 and 30 weeks postpartum but somewhat lower TWT in the CTRL group at week 18, with a moderate Cohen-d effect (d=0.48).

The results for the diary-based measures of wakefulness at night are more nuanced. The two mixed effect models revealed that, although there was no difference between the groups in time awake caring for the infant (TWT_{infant}; p-values for main group effect and its interaction with each of the slopes were > .3), there was a trend for the CBTI group to report less time awake excluding time caring for the infant (TWT_{other}; $p = .094$). Examining the times awake at each of the three timepoints revealed similarly divergent patterns. The groups did not differ in time awake for infant care at any of the three timepoints (d=0.08 - 0.18) but time awake excluding infant care (TWT_{other}) was significantly lower for CBTI participants at each time point: by 25 minutes at 8 weeks (d=0.65), 28 minutes at 18 weeks (d=0.47) and 18 minutes at 30 weeks postpartum (d=0.53). Among both groups, time caring for the infant (TWT_{infant}) decreased by an average of 45 minutes from 8 to 18 weeks and continued to decrease by about 10 minutes from 18 to 30 weeks postpartum ($p = .010$). Time awake excluding time caring for the infant (TWT_{other}) changed relatively little, increasing by about 5 minutes from week 8 to 18 and then decreasing by about 10 minutes from week 18 to 30

Exploratory analyses examining the role of changes in insomnia severity during pregnancy on postpartum insomnia trajectories showed a moderation effect; the three-way interaction between the change in ISI from baseline to after last pregnancy session, group, and each of the two slopes ($p = .055$ fo Slope 1 and $p = .038$ for Slope 2). **Figure 2** illustrates simple slopes for those who had at least 50% reduction in ISI scores from baseline to the end of the pregnancy treatment phase to those who did not. For those who had < 50% reduction on pregnancy ISI scores (depicted in gray in **Figure 2**), postpartum ISI scores were elevated (mean > 7) at all three time points regardless of group allocation. Among participants who had >= 50% reduction on pregnancy ISI scores (depicted in black in **Figure 2**), those

allocated to CBTI group showed consistently stable ISI scores (mean < 6) over time, whilst those allocated to the CTRL group had variable ISI scores over time with large individual differences.

DISCUSSION

The current study investigated the effectiveness of CBTI delivered during pregnancy and postpartum on insomnia severity (the primary outcome) and nighttime wakefulness during the postpartum period. Although, as we, and others, previously reported, CBTI reduces insomnia severity during pregnancy relative to a control intervention, we found no significant main group effects nor interaction between group allocation and time during the postpartum period. However, examining the pattern of change in insomnia severity across the 30 weeks assessment period reveals that, although the ISI did not differ between groups at 8 and 18 weeks postpartum, women assigned to CBTI had lower insomnia severity at 30 weeks after childbirth. As depicted in **Figure 2**, the trajectory of change was such that, whereas those assigned to control experienced an increase in ISI scores from 18 to 30 weeks, those assigned to CBTI did not.

In interpreting these results, it is important to consider the profound reduction in sleep opportunity that many women experience during the first few postnatal months, which likely results in a very strong homeostatic sleep drive that could facilitate falling and returning to sleep and may overshadow the benefits derived from CBTI. Others have similarly found that the benefits of prenatal CBTI on maternal postpartum insomnia are absent early during the postpartum period and become more apparent later, when maternal and infant sleep begin to decouple and consequently when postpartum moms are perhaps less sleep deprived.[17, 34]

Importantly, our exploratory moderation analyses suggest that women who experienced at least 50% reduction in insomnia severity during pregnancy experienced a more stable and lower insomnia severity during the initial 30-week postpartum period. Specifically, among participants who had at least 50% reduction in pregnancy ISI scores, those allocated to CBTI group showed consistently stable ISI scores (mean < 6) over time, whilst those allocated to the CTRL group had variable ISI scores over time during the postpartum period, with large individual differences. The stability of sleep patterns may reflect the ability of women in the CBTI group to utilize treatment tools that contribute to the maintenance of more consistently good sleep patterns.

Recognizing the profound effects of infant sleep on maternal sleep during the initial postpartum months, we asked women to report separately on the time they were awake taking care of the infant and the time they were awake unrelated to infant care. We found that although time spent in the middle of the night caring for the infant did not differ by treatment group, time awake excluding time caring for infant was shorter among those assigned to CBTI than those assigned to the CTRL groups at all three timepoints (8, 18, and 30 weeks postpartum) with a difference of nearly 30 minutes between the two groups at 18 weeks. It is possible that skills learned in CBTI have helped women who received CBTI to fall back asleep faster after disruptions caused by their infants and to experience fewer awakenings unrelated to infant care. This is consistent with a finding by Bei and colleagues, who reported that, compared to a control intervention, CBTI was associated with lower insomnia symptoms during the first year of postpartum period among participants with elevated insomnia symptoms during the third trimester.[34] Our findings highlight the value of tailoring sleep assessment for individuals when unavoidable external circumstances outside of one's control disrupt sleep, such as infant or elder care at night, or on call work duties at night. For example, Billings (2022) suggested the use of tailoring the traditional sleep diary to address specific job-related characteristics in the fire and emergency service occupation, where multiple sleep episodes in a single night may result from disruption of sleep in response to emergencies.[35]

Our study did not find group differences with actigraphy TWT during the postpartum period. Reasons for null findings may be due to two possibilities. First, the actigraphy-based measure of TWT includes both time awake caring for the infant and time awake for other reasons. Second, it is not unusual to find a discrepancy in findings for objective and subjective sleep in intervention studies, including

among women during pregnancy. Consistent with our findings, a meta-analysis of studies on the effectiveness of CBTI in general samples documented clear benefits of CBTI on subjective sleep parameters[SA1] but no reliable reduction on actigraphy measures of TWT.[36] Another meta-analysis by Okajima et al. (2011) reached similar conclusions.[37] Specific to pregnancy, a study of a mindfulness-based cognitive intervention to improve sleep during pregnancy also found divergence of subjective and objective results, reporting significant changes in sleep efficiency derived from sleep diaries but not from actigraphy.[38]

In interpreting the absence of effects of the sleep intervention on postpartum depression severity in our study, one needs to consider the fact that overall depression scores across all time points were relatively low, likely due to the fact that we excluded participants who met criteria for depression during pregnancy. Results of research examining the effects of CBTI on depressive symptoms during the postpartum among women who experienced insomnia disorder during pregnancy have been mixed. It appears that one other study that had a control insomnia intervention found no effect of CBTI delivered during pregnancy on postpartum depression, whereas one study comparing the intervention to treatment as usual did find an effect. Specifically, consistent with our study, in which women received CBTI from a therapist, Kalmbach and colleagues (2020) found no difference in depression scores at six weeks after childbirth between women receiving digital CBTI and women receiving a digital control intervention during pregnancy.[14] In contrast, Felder and colleagues (2022) found greater improvements in depression symptom severity from baseline to 3 months postpartum among women who received digital CBTI during pregnancy compared to women receiving treatment as usual.[17] Thus, for individuals without depression during pregnancy, positive s of CBTI delivered during pregnancy on depression symptom severity during the postpartum were detected in absence of control for non-specific therapeutic factors. To the best of our knowledge, there are no studies on the effects of CBTI on depression severity among women who are experiencing depression during pregnancy.

Our study has a few limitations that underscore a need for caution in interpreting our results and consideration that findings are hypothesis generating rather than definitive. First, the sample analyzed in this study differed from the initial randomized sample in that participants who provided postpartum data for this study had lower ISI score at baseline, were more likely to be Caucasian, and less likely to have low household income. This means that the sample was no longer representative of the original study. While there were no differences between those who were and were not included in the analyzable sample in allocation of treatment arm, the results should be considered exploratory in nature. A second limitation is that actigraphy has not yet been validated for use during pregnancy, a time when fetal movement and increased leg movements might be registered as wakefulness. We also note that we cannot infer from these results whether CBTI will be effective for prenatal sleep disturbances that do not meet the diagnostic threshold for insomnia disorder.

CONCLUSIONS

The current study investigated the effectiveness of CBTI delivered during pregnancy, plus one postpartum session, on insomnia severity and nighttime wakefulness during the postpartum period. Receiving CBTI was associated with less time awake at night that was not related to infant care and lower insomnia severity at 30 weeks postpartum, when the newborn typically places less demands on maternal sleep and the mother is likely to be less sleep deprived compared to earlier in the postpartum period. We believe these benefits outweigh the potential transient daytime sleepiness associated with the initial restriction of time in maternal bed. We note that to minimize maternal sleep deprivation, the CBTI protocol used in this study was modified both during pregnancy and during the postpartum period. Our findings underscore the importance of treating insomnia during pregnancy, a conclusion that is further supported by our finding that pregnant women who responded to insomnia treatment during pregnancy experienced better sleep in the postpartum period.

ABBREVIATIONS

CBTI, cognitive behavioral therapy for insomnia
CTRL, control
ISI, Insomnia Severity Index
RCT, randomized controlled trial
SE, sleep efficiency
SOL, sleep onset latency
TIB, time in bed
TST, total sleep time
TWT, total wake time

ACKNOWLEDGEMENTS

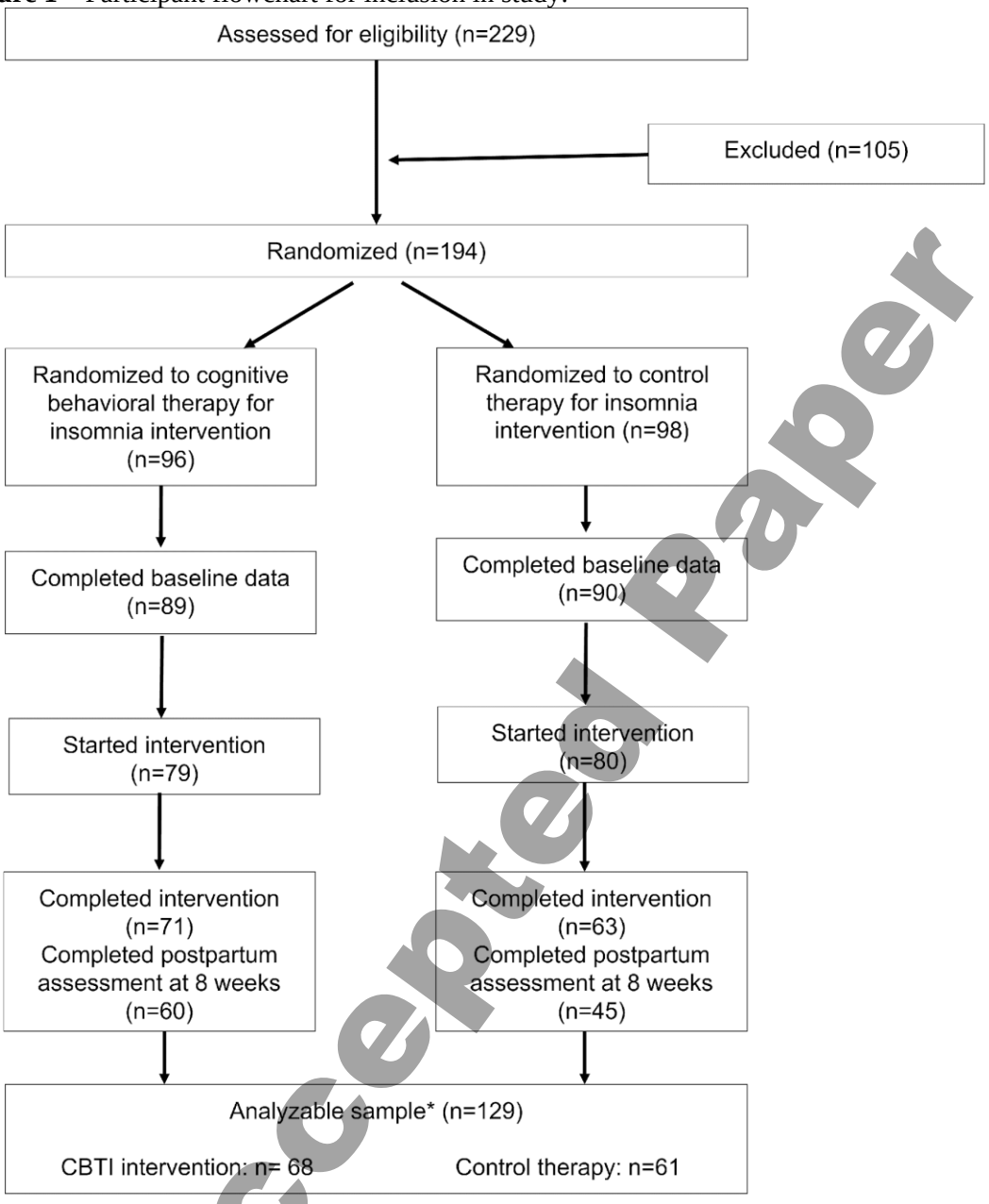
Some of the results were presented at SLEEP 2019 and SLEEP 2020 meetings. The authors thank the following individuals for their valuable support of the project's implementation: Haddas Elisha, PA, Michelle Reade, BA, Donn Posner, PhD and the study therapists.

REFERENCES

1. Facco FL, Kramer J, Ho KH, Zee PC, Grobman WA. Sleep disturbances in pregnancy. *Obstet Gynecol*. 2010;115(1):77-83.
2. Kalmbach DA, Cheng P, Roth A, et al. DSM-5 insomnia disorder in pregnancy: associations with depression, suicidal ideation, and cognitive and somatic arousal, and identifying clinical cutoffs for detection. *SLEEP Adv*. 2022;3(1).
3. Román-Gálvez R, Amezcua-Prieto C, Salcedo-Bellido I, Martínez-Galiano J, Khan K, Bueno-Cavanillas A. Factors associated with insomnia in pregnancy: A prospective Cohort Study. *Eur J Obstet Gynecol Reprod Biol*. 2018;221:70-75.
4. Sivertsen B, Hysing M, Dørheim SK, Eberhard-Gran M. Trajectories of maternal sleep problems before and after childbirth: a longitudinal population-based study. *BMC Pregnancy Childbirth*. 2015;15(1):1-8.
5. Quin N, Lee JJ, Pinnington DM, Newman L, Manber R, Bei B. Differentiating perinatal Insomnia Disorder and sleep disruption: a longitudinal study from pregnancy to 2 years postpartum. *Sleep*. 2022;45(2).
6. Malish S, Arastu F, O'Brien LM. A preliminary study of new parents, sleep disruption, and driving: a population at risk? *Matern Child Health J*. 2016;20(2):290-97.
7. Bei B, Milgrom J, Ericksen J, Trinder J. Subjective perception of sleep, but not its objective quality, is associated with immediate postpartum mood disturbances in healthy women. *Sleep*. 2010;33(4):531-38.
8. Wilson N, Wynter K, Fisher J, Bei B. Related but different: distinguishing postpartum depression and fatigue among women seeking help for unsettled infant behaviours. *BMC Psychiatry*. 2018;18(1):1-9.
9. Coo Calcagni S, Bei B, Milgrom J, Trinder J. The relationship between sleep and mood in first-time and experienced mothers. *Behav Sleep Med*. 2012;10(3):167-79.
10. Swanson LM, Pickett SM, Flynn H, Armitage R. Relationships among depression, anxiety, and insomnia symptoms in perinatal women seeking mental health treatment. *J Womens Health*. 2011;20(4):553-58.
11. Sharma V, Mazmanian D. Sleep loss and postpartum psychosis. *Bipolar Disord*. 2003;5(2):98-105.
12. Emamian F, Khazaie H, Okun ML, Tahmasian M, Sepehry AA. Link between insomnia and perinatal depressive symptoms: A meta- analysis. *J Sleep Res*. 2019;28(6):e12858.
13. Manber R, Bei B, Simpson N, et al. Cognitive behavioral therapy for prenatal insomnia: a randomized controlled trial. *Obstet Gynecol*. 2019;133(5):911.
14. Kalmbach DA, Cheng P, O'Brien LM, et al. A randomized controlled trial of digital cognitive behavioral therapy for insomnia in pregnant women. *Sleep Med*. 2020;72:82-92.
15. Felder JN, Epel ES, Neuhaus J, Krystal AD, Prather AA. Efficacy of digital cognitive behavioral therapy for the treatment of insomnia symptoms among pregnant women: a randomized clinical trial. *JAMA Psychiatry*. 2020;77(5):484-92.
16. Kalmbach DA, Cheng P, Roth T, et al. Examining patient feedback and the role of cognitive arousal in treatment non-response to digital cognitive-behavioral therapy for insomnia during pregnancy. *Behav Sleep Med*. 2022;20(2):143-63.
17. Felder JN, Epel ES, Neuhaus J, Krystal AD, Prather AA. Randomized controlled trial of digital cognitive behavior therapy for prenatal insomnia symptoms: effects on postpartum insomnia and mental health. *Sleep*. 2022;45(2):zsab280.
18. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders.* 5th ed. Washington D.C.: 2013.
19. Edinger JD, Wyatt JK, Stepanski EJ, et al. Testing the reliability and validity of DSM-IV-TR and ICSD-2 insomnia diagnoses: results of a multitrait-multimethod analysis. *Arch Gen Psychiatry*. 2011;68(10):992-1002.

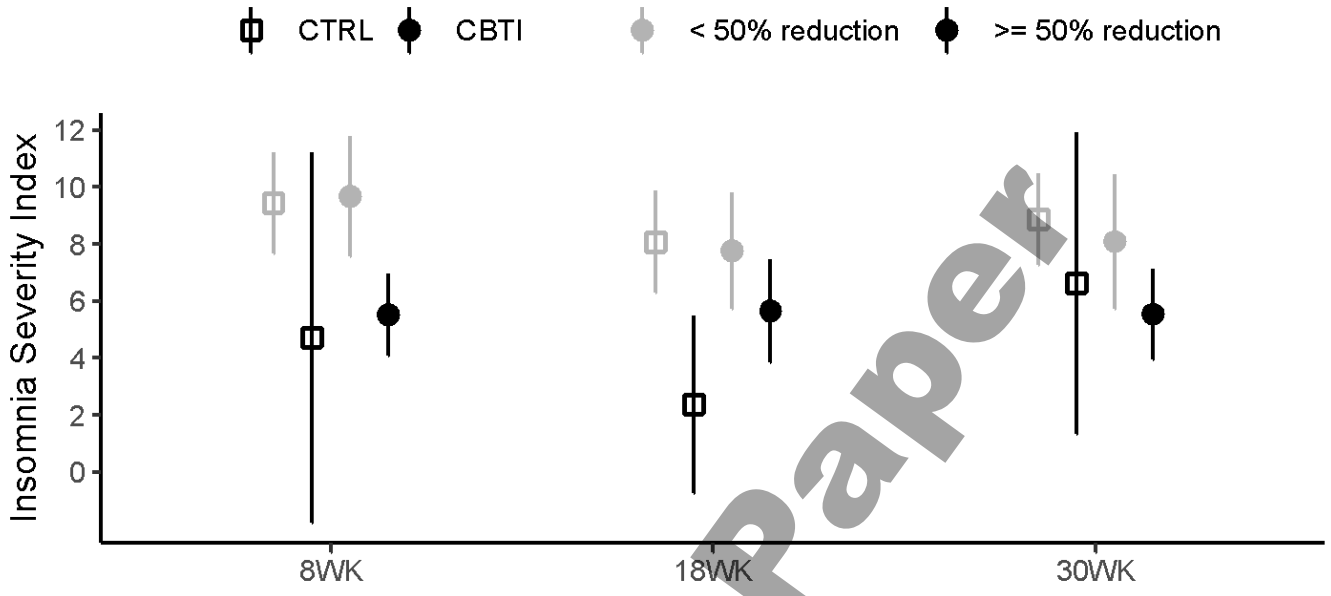
20. Efird J. Blocked randomization with randomly selected block sizes. *Int J Environ Res Public Health*. 2011;8(1):15-20.
21. Spielman AJ, Saskin P, Thorpy MJ. Treatment of chronic insomnia by restriction of time in bed. *Sleep*. 1987;10(1):45-56.
22. Lichstein KL, Morin CM. *Treatment of late-life insomnia*. Sage; 2000.
23. Stremler R, Hodnett E, Kenton L, et al. Effect of behavioural-educational intervention on sleep for primiparous women and their infants in early postpartum: multisite randomised controlled trial. *BMJ*. 2013;346.
24. Edinger JD, Wohlgemuth WK, Radtke RA, Marsh GR, Quillian RE. Cognitive behavioral therapy for treatment of chronic primary insomnia: a randomized controlled trial. *JAMA*. 2001;285(14):1856-64.
25. Manber R, Buysse DJ, Edinger J, et al. Efficacy of cognitive-behavioral therapy for insomnia combined with antidepressant pharmacotherapy in patients with comorbid depression and insomnia: a randomized controlled trial. *J Clin Psychiatry*. 2016;77(10):2446.
26. Manber R, Edinger JD, Gress JL, Pedro-Salcedo MGS, Kuo TF, Kalista T. Cognitive behavioral therapy for insomnia enhances depression outcome in patients with comorbid major depressive disorder and insomnia. *Sleep*. 2008;31(4):489-95.
27. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry*. 1998;59(20):22-33.
28. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Med*. 2001;2(4):297-307.
29. Morin CM, Belleville G, Bélanger L, Ivers H. The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep*. 2011;34(5):601-08.
30. Carney CE, Buysse DJ, Ancoli-Israel S, et al. The consensus sleep diary: standardizing prospective sleep self-monitoring. *Sleep*. 2012;35(2):287-302.
31. R Core Team R. *R: A Language and Environment for Statistical Computing.* R Foundation for Statistical Computing, Vienna, Austria; 2018.
32. Cohen J. *Statistical Power Analysis for the Behavioral Sciences.* Routledge; 1988.
33. Nunes EV, Pavlicova M, Hu M-C, et al. Baseline matters: The importance of covariation for baseline severity in the analysis of clinical trials. *Am J Drug Alcohol Abuse*. 2011;37(5):446-52.
34. Bei B, Pinnington DM, Quin N, et al. Improving perinatal sleep via a scalable cognitive behavioural intervention: findings from a randomised controlled trial from pregnancy to 2 years postpartum. *Psychol Med*. 2021:1-11.
35. Billings JM. Firefighter sleep: a pilot study of the agreement between actigraphy and self-reported sleep measures. *J Clin Sleep Med*. 2022;18(1):109-17.
36. Mitchell LJ, Bisdounis L, Ballesio A, Omlin X, Kyle SD. The impact of cognitive behavioural therapy for insomnia on objective sleep parameters: A meta-analysis and systematic review. *Sleep Med Rev*. 2019;47:90-102.
37. Okajima I, Komada Y, Inoue Y. A meta-analysis on the treatment effectiveness of cognitive behavioral therapy for primary insomnia. *Sleep Biol Rhythms*. 2011;9(1):24-34.
38. MacKinnon D, Karlsen A, Dawley S, Steen M, Afewerki S, Kenzhegaliyeva A. Legitimation, institutions and regional path creation: A cross-national study of offshore wind. *Reg Stud*. 2022;56(4):644-55.

Figure 1—Participant flowchart for inclusion in study.



*Analyzable sample consisted of all participants who completed at least one postpartum assessment

Figure 2—Simple slopes for participants with <50% and >=50% reduction in Insomnia Severity Index scores from baseline to end of pregnancy treatment.



Mean and 95% confidence intervals are shown. 8wk, 18wk, and 30wk represent 8, 18, and 30 weeks postpartum time points.

Table 1—Demographic and symptom summary at time of study enrollment.

	Overall	CBTI	Control
n (%)	129 (100)	68 (52.7)	61 (47.3)
Age, M (SD)	33.45 (4.99)	33.65 (5.03)	33.22 (4.99)
Nulliparas, n (%)	76 (58.9)	40 (58.8)	36 (59.0)
Race, n (%)			
White	73 (56.6)	41 (60.3)	32 (52.5)
Asian	21 (16.3)	9 (13.2)	12 (19.7)
Black	4 (3.1)	3 (4.4)	1 (1.6)
Other	27 (20.9)	14 (20.6)	13 (21.3)
Unknown	4 (3.1)	1 (1.5)	3 (4.9)
Annual household income < $55k, n (%)	36 (30.0)	15 (23.8)	21 (36.8)
Gestation at baseline*, M (SD)	24.68 (5.07)	25.14 (5.03)	24.17 (5.10)
EPDS at baseline, M (SD)	8.40 (4.34)	7.71 (4.30)	9.18 (4.28)
ISI at baseline, M (SD)	15.46 (4.41)	15.40 (4.32)	15.52 (4.55)
ISI after pregnancy Intervention, M (SD)	8.96 (5.04)	7.54 (4.95)	10.59 (4.68)

Sample are participants who provided at least one postpartum measure of the ISI, actigraphy, or sleep diary. *unit = weeks.

ISI: Insomnia Severity Index, EPDS: Edinburgh Postnatal Depression Scale.

Table 2—Descriptive statistics for self-reported and actigraphy assessed sleep variables.

	Overall	CBTI	Control	Group Difference: *t*(*df*), *P*, *d*
Insomnia Severity Index				
8wk	7.86 (5.45)	7.25 (5.02)	8.67 (5.93)	1.32 (103), .189, .26
18wk	6.81 (5.03)	6.61 (4.68)	7.02 (5.43)	.39 (92), .695, .08
30wk	7.54 (5.23)	6.59 (5.05)	8.70 (5.27)	2.06 (100), .042, .41
Actigraphy TWT (minutes)				
8wk	115.65 (39.42)	116.93 (42.74)	113.90 (35.03)	-.32 (69), .752, .08
18wk	86.17 (31.54)	94.10 (33.60)	79.20 (28.31)	-1.89 (60), .063, 0.48
30wk	95.88 (39.44)	92.88 (44.79)	98.88 (33.71)	0.61 (62), .547, 0.15
Sleep diary TWT_{other} (minutes)				
8wk	43.26 (40.72)	32.26 (27.66)	57.40 (49.83)	3.39 (110), <.001, 0.65
18wk	48.73 (60.35)	35.56 (28.68)	63.28 (80.31)	2.10 (78), .039, 0.47
30wk	38.55 (35.57)	30.56 (32.78)	48.93 (36.79)	2.43 (83), .017, 0.53
Sleep diary TWT_{infant} (minutes)				
8wk	83.98 (48.20)	80.21 (43.93)	88.73 (53.17)	0.93 (111), .353, 0.18
18wk	37.48 (28.71)	38.59 (30.02)	36.26 (27.54)	-0.36 (78), .719, 0.08
30wk	33.34 (27.04)	32.42 (27.71)	34.52 (26.47)	0.35 (83), .726, 0.08
Edinburgh Postnatal Depression Scale				
8wk	5.13(4.23)	4.85(4.01)	5.51(4.53)	.79(103), .431, .16
18wk	4.96(4.31)	4.27(3.51)	5.71(4.97)	1.64(92), .104, .34
30wk	5.23 (4.42)	4.99 (4.45)	5.52 (4.43)	0.60(100), .549, .12

TWT_{other} = time awake excluding time caring for infant; TWT_{infant} = time awake to care for infant.

Table 3—Summary of linear mixed effects models on group differences in postpartum insomnia trajectories.

	Insomnia Severity Index	**Diary - TWT_{other}**	**Diary - TWT_{infant}**	**Actigraphy TWT**
Intercept	2.52 [-0.43, 5.47], 0.093	35.09 [22.69, 47.48], <.001	42.29 [34.54, 50.03], <.001	44.93 [28.35, 61.5], <.001
Slope 1	0.97 [0.06, 1.88], 0.036*	0.86 [-7.67, 9.38], 0.843	41.34 [34.63, 48.05], <.001***	31.37 [20.89, 41.86], <.001***
Slope 2	0.62 [-0.29, 1.53], 0.183	-0.79 [-9.53, 7.95], 0.859	-9.29 [-16.31, -2.27], 0.010 *	11.12 [0.44, 21.79], 0.041*
Group	-0.41 [-2.37, 1.55], 0.677	-13.46 [-29.22, 2.31], 0.094†	-7.28 [-22.79, 8.24], 0.355	9.55 [-7.11, 26.21], 0.258
Slope 1 × Group	-1.33 [-3.15, 0.49], 0.152	-2.82 [-19.87, 14.23], 0.744	-0.54 [-13.96, 12.88], 0.937	-13.56 [-34.52, 7.41], 0.202
Slope 2 × Group	-1.55 [-3.37, 0.27], 0.095†	-5.79 [-23.27, 11.69], 0.514	4.66 [-9.37, 18.7], 0.512	-17.1 [-38.45, 4.25], 0.115
Baseline value	0.29 [0.11, 0.47], 0.002**	0.08 [-0.03, 0.19], 0.141	Not applicable	0.45 [0.3, 0.61], <.001***
Observation	301	269	278	194
Sample size	117	122	126	95

Unstandardized coefficients [95% confidence intervals], p-value are presented. TWT: total wake time (minutes). Slope 1: 8 weeks vs 18 weeks postpartum, positive values indicate 8 weeks values larger than 18 weeks; Slope 2: 30 weeks vs 18 weeks postpartum, positive values indicate 30 weeks value larger than 18 weeks value. For Group, CBTI is coded as 0.5 and CTRL -0.5, such that coefficients are interpreted as values for overall sample. †p<.1, *p<.05, **p<.01, ***p<.001.

TWTother = time awake excluding time caring for infant; TWTinfant = time awake to care for infant; TWT = Total Wake Ti.