



JAMA Psychiatry. 2020 May; 77(5): 1–9.

PMCID: PMC6990703

Published online 2020 Jan 22. doi: 10.1001/jamapsychiatry.2019.4491:

PMID: [31968068](#)

[10.1001/jamapsychiatry.2019.4491](#)

Efficacy of Digital Cognitive Behavioral Therapy for the Treatment of Insomnia Symptoms Among Pregnant Women

A Randomized Clinical Trial

[Jennifer N. Felder](#), PhD,^{1,2} [Elissa S. Epel](#), PhD,^{2,3} [John Neuhaus](#), PhD,⁴ [Andrew D. Krystal](#), MD, MS,² and [Aric A. Prather](#), PhD^{2,3}

¹Osher Center for Integrative Medicine, University of California, San Francisco, San Francisco

²Department of Psychiatry, University of California, San Francisco, San Francisco

³Center for Health and Community, University of California, San Francisco, San Francisco

⁴Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco

✉ Corresponding author.

[Article Information](#)

Accepted for Publication: November 12, 2019.

Corresponding Author: Jennifer N. Felder, PhD, Osher Center for Integrative Medicine, University of California, San Francisco, 1545 Divisadero St, PO Box 1726, San Francisco, CA 94115 (jennifer.felder@ucsf.edu).

Published Online: January 22, 2020. doi:10.1001/jamapsychiatry.2019.4491

Correction: This article was corrected on April 22, 2020, to update the Conflict of Interest Disclosures section.

Author Contributions: Dr Felder had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Felder, Epel, Prather.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Felder, Neuhaus, Krystal.

Critical revision of the manuscript for important intellectual content: Felder, Epel, Neuhaus, Prather.

Statistical analysis: Felder, Neuhaus.

Obtained funding: Felder.

Administrative, technical, or material support: Felder.

Supervision: Epel, Krystal, Prather.

Conflict of Interest Disclosures: Dr Felder reported receiving voucher codes for Sleepio, the digital cognitive behavioral therapy for insomnia intervention, from Big Health. All authors reported receiving grants from the National Institutes of Health during the conduct of the study. Dr Krystal reported receiving grants from Janssen Pharmaceuticals, Axsome Therapeutics, Reveal Biosensors, and the National Institutes of Health and personal fees from Adare, Axsome Therapeutics, Eisai, Ferring Pharmaceuticals, Galderma, Harmony Biosciences, Janssen Pharmaceuticals, Jazz Pharmaceuticals, Millennium Pharmaceuticals, Merck, Neurocrine Biosciences, Otsuka Pharmaceuticals, Pernix, Reveal Biosensors, and Takeda outside the submitted work. Dr Prather reported receiving grants from Headspace outside the submitted work. Dr Epel reported that she is a scientific advisor to Meru Health. No other disclosures were reported.

Funding/Support: The research was supported by the University of California, San Francisco, California Preterm Birth Initiative transdisciplinary postdoctoral fellowship, which was funded by grant OPP1107312 from the Bill & Melinda Gates Foundation and a donation from Marc and Lynne Benioff. This study was supported by grant UL1 TR001872 from the National Center for

Advancing Translational Sciences, National Institutes of Health; grant K23AT009896 from the National Center for Complementary and Integrative Health (Dr Felder); grant T32MH019391 from the National Institute of Mental Health (Dr Felder); grant KL2 TR001870 from the National Center for Advancing Translational Sciences (Dr Neuhaus); and grant R01HL142051 from the National Heart, Lung, and Blood Institute (Dr Prather).

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See [Supplement 3](#).

Additional Contributions: Alison Hartman, BA, of the Center for Health and Community at the University of California, San Francisco, and Esperanza Castillo, MS, and Brianne Taylor, AA, of the California Preterm Birth Initiative at the University of California, San Francisco, were project coordinators and assisted with recruitment, enrollment, and data collection. Danielle Roubinov, PhD, of the Department of Psychiatry at the University of California, San Francisco, generated the randomization sequence. Alinne Barrera, PhD, of Palo Alto University, served as an independent safety officer. We are deeply grateful for the women who volunteered their time to participate in this research. No compensation was received.

Received 2019 Sep 10; Accepted 2019 Nov 12.

[Copyright](#) 2020 American Medical Association. All Rights Reserved.

Key Points

Question

What is the efficacy of digital cognitive behavioral therapy compared with standard treatment among pregnant women with insomnia symptoms?

Findings

In this randomized clinical trial of 208 pregnant women with insomnia symptoms, digital cognitive behavioral therapy for the treatment of insomnia was associated with statistically significantly greater improvements in insomnia symptom severity, sleep efficiency, global sleep quality, insomnia caseness, depressive symptoms, and anxiety symptoms compared with standard treatment.

Meaning

Digital cognitive behavioral therapy is an effective, scalable, safe, and acceptable intervention for improving insomnia symptoms during pregnancy.

Abstract

Importance

Despite the prevalence and adverse consequences of prenatal insomnia, a paucity of research is available regarding interventions to improve insomnia symptoms during pregnancy.

Objective

To test the efficacy of digital cognitive behavioral therapy for insomnia (CBT-I) compared with standard treatment among pregnant women with insomnia symptoms.

Design, Setting, and Participants

This randomized clinical trial enrolled pregnant women from November 23, 2016, to May 22, 2018. Of the 2258 women assessed for eligibility using an online self-report questionnaire, 208 were randomized to receive digital CBT-I ($n = 105$) or standard treatment ($n = 103$) for insomnia. Participants were pregnant up to 28 weeks' gestation, and they either had elevated insomnia symptom severity or met the criteria for insomnia caseness as determined by self-report questionnaires. Participants completed outcome measures at 10 weeks (postintervention) and 18 weeks (follow-up) after randomization. All study visits were completed remotely, and the intervention was delivered digitally. Data were analyzed between December 12, 2018, and July 2, 2019.

Interventions

Digital CBT-I consisted of 6 weekly sessions of approximately 20 minutes each. Standard treatment reflected standard care. Women receiving standard treatment had no limits placed on the receipt of nonstudy treatments, including medication and psychotherapy.

Main Outcomes and Measures

All outcomes were assessed remotely using self-report questionnaires administered via online survey. The primary outcome was the change in insomnia symptom severity (measured by the Insomnia Severity Index) from baseline to postintervention. Secondary outcomes were sleep efficiency and nightly sleep duration (defined by sleep diary), global sleep quality (measured by the Pittsburgh Sleep Quality Index), depressive symptom severity (measured by the Edinburgh Postnatal Depression Scale), and anxiety symptom severity (measured by the Generalized Anxiety Disorder Scale-7). For each outcome, we also examined the change from baseline to follow-up.

Results

The 208 participants had a mean (SD) age of 33.6 (3.7) years and a mean (SD) gestational age of 17.6 (6.3) weeks at baseline. Most of the participants were white (138 [66.3%]), married or cohabiting (196 [94.2%]), had a college degree (180 [86.5%]), and earned \$100 000 or more per year (141 [67.8%]). Women randomized to receive digital CBT-I experienced statistically significantly greater improvements in insomnia symptom severity from baseline to postintervention compared with women randomized to receive standard treatment (time-by-group interaction, difference = -0.36; 95% CI, -0.48 to -0.23; $\chi^2 = 29.8$; $P < .001$; $d = -1.03$). Improvements from baseline to postintervention for all secondary outcomes, with the exception of sleep duration, were statistically significant. A similar pattern of results was evident for the change from baseline to follow-up.

Conclusions and Relevance

In this trial, digital CBT was an effective, scalable, safe, and acceptable intervention for improving insomnia symptoms during pregnancy.

Trial Registration

ClinicalTrials.gov identifier: [NCT02805998](#)

This randomized clinical trial examines the efficacy of digital cognitive behavioral therapy for insomnia compared with standard treatment among pregnant women with insomnia symptoms.

Introduction

Insomnia symptoms are prevalent during pregnancy, with as many as 1 in 7 pregnant women reporting moderate to severe symptoms.¹ Although sleep disturbance during pregnancy may be viewed as normative and innocuous, research indicates that it is associated with an increased risk of adverse maternal outcomes, including depression and preterm birth.^{2,3} Limited research is available on interventions to improve insomnia symptoms during pregnancy. A robust body of literature documents the efficacy of cognitive behavioral therapy for insomnia (CBT-I) across a variety of populations,⁴ and it is recommended as the first line treatment by the American College of Physicians.⁵ Cognitive behavioral therapy for insomnia that is delivered in person by a trained clinician is effective for pregnant women diagnosed with insomnia disorder.⁶ Although CBT-I is efficacious, demand for the treatment exceeds the availability of trained clinicians.⁷ Clinical innovation has attempted to bridge this science-care gap with digital adaptations, which are effective among nonpregnant populations.^{8,9} A digital CBT-I program may be of particular interest for pregnant women, who report a preference for mental health care that includes flexible options¹⁰ and for whom timely intervention may be particularly important.

We conducted a randomized clinical trial to evaluate digital CBT-I compared with standard treatment among 208 pregnant women with elevated insomnia symptoms. First, we hypothesized that compared with women randomized to receive standard treatment, women randomized to receive digital CBT-I would experience greater improvements from baseline to postintervention (ie, 10 weeks after randomization) in subjective sleep outcomes, including insomnia symptom severity (the primary outcome, which was measured by the Insomnia Severity Index [ISI]), diary-defined sleep efficiency and duration, global sleep quality, and insomnia caseness. Second, because poor sleep is associated with increased depressive and anxiety symptoms among perinatal women^{11,12,13} and digital CBT-I is associated with improvements in depressive and anxiety symptoms,^{14,15} we hypothesized that digital CBT-I would be effective in reducing depressive and anxiety symptoms among pregnant women. For all outcomes, we also investigated the change from baseline to follow-up (ie, 18 weeks after randomization).

Methods

Participants

Participants were enrolled from November 23, 2016, through May 22, 2018. Pregnant women were recruited using conventional passive recruitment methods (eg, flyers hung in retail stores), a national health volunteer registry, social media advertisements, and word of mouth. In addition, patients at a university hospital were recruited via messages sent through the electronic health record and direct mail and via electronic flyers in the obstetrics and gynecology waiting rooms.

The inclusion criteria were (1) self-reported pregnancy up to 28 weeks' gestation; (2) 18 years or older; (3) met the *DSM-5* criteria for insomnia disorder, as determined by the Sleep Condition Indicator^{16,17} (SCI) (women experiencing symptoms for ≥ 1 month were eligible, in contrast to the *DSM-5* criteria requiring symptom duration of ≥ 3 months, to include women whose symptoms began during pregnancy) or experienced elevated insomnia symptom severity, as determined by a total score of 11 or greater on the ISI;^{18,19} and (4) had regular access to a web-enabled computer, tablet, or smart phone. The exclusion criteria were (1) probable major depression, as determined by a total score of 15 or greater on the Edinburgh Postnatal Depression Scale (EPDS);²⁰ (2) self-reported bipolar disorder; (3) self-reported history of psychosis; (4) active suicidality, defined as a score greater than 1 on item 10 of the EPDS, which assesses thoughts of self-harm, or report of a specific suicide plan or recent suicide attempt; and (5) a shift-work employee.

Design

Participants were randomly assigned to receive digital CBT-I or standard treatment, with a waiting list control. Although we used a 1:1 allocation ratio with blocked randomization to balance the group sizes, an error in how condition assignments were recorded resulted in 105 participants randomized to the digital CBT-I group and 103 participants randomized to the standard treatment group. For study administration purposes, staff members were unblinded. However, all outcome measures were participant-reported, potentially mitigating the consequences of staff unblinding on the outcome assessment. Participants were unblinded because of the nature of the comparison group, which was not an active comparator. The study statistician remained blinded to condition assignments for all primary analyses.

The study received approval from the institutional review board of the University of California, San Francisco, and all participants provided electronic informed consent. The trial protocol is available in [Supplement 1](#), and changes made to the eligibility criteria after the study began are available in eMethods in [Supplement 2](#).

Interventions

The digital CBT-I program, Sleepio (Big Health), has been described in detail in other publications.^{8,21} In brief, digital CBT-I was delivered through 6 weekly sessions that were accessed via website or iOS app. The treatment content was based on CBT-I manuals and included 5 main components: sleep restriction, stimulus control, cognitive therapy, relaxation techniques, and sleep hygiene and education.²² The program was interactive and delivered by an animated digital therapist. Participants received automated reminders to complete each session and a daily sleep diary, and they received tailored, automated help based on their progress. Participants had access to a moderated online community and a library of sleep information.

The control group received standard care for prenatal patients with insomnia. Standard care comprised a range of nonstudy treatments, including sleep, pain, and antidepressant medications (both prescribed and over-the-counter); alternative therapy or herbal supplements; psychotherapy or counseling; and support groups. No limits were placed on the receipt of nonstudy treatments. Participants randomized to the standard treatment group received a free voucher code to access the Sleepio program at study completion.

Outcomes

Subjective Sleep Outcomes The primary outcome for the study was the total score on the ISI,^{18,19} which is a 7-item syndromal measure of insomnia that assesses difficulty with initiating or maintaining sleep, satisfaction with sleep, impairment, distress, and the extent to which others have noticed symptoms during the previous 2 weeks. Total scores of 7 or less indicate no clinically significant insomnia, 8 to 14 indicate subthreshold insomnia, 15 to 21 indicate moderate insomnia, and 22 or greater indicate severe insomnia. A cutoff of 11 has been validated to identify participants for clinical trials.²³ As in previous research with pregnant women,⁶ we defined remission as a total ISI score of 7 or less.

Daily sleep diaries were used to measure sleep efficiency and duration. Sleep efficiency was calculated by dividing the amount of time sleeping in bed by the total amount of time spent in bed and multiplying the quotient by 100. Scores ranged from 0% to 100%, with 85% or higher considered normal. Sleep duration was defined as the total amount of nightly sleep in hours. Global sleep quality was measured using the Pittsburgh Sleep Quality Index, a 19-item instrument comprised of 7 components that assess sleep duration,

disturbance, latency, efficiency, quality, days of dysfunction because of sleepiness, and the need for medication to sleep.²⁴ Each component score ranges from 0 to 3, and the components are summed to create a Pittsburgh Sleep Quality Index global sleep quality score ranging from 0 to 21. Higher scores indicate worse global sleep quality, and scores greater than 5 indicate poor sleep. To determine whether participants met diagnostic criteria for insomnia, we used the SCI. Consistent with previous research,²⁵ we added a ninth item to assess early morning awakening, which is a symptom of insomnia disorder included in the *DSM-5*.

Mental Health Outcomes Depressive symptom severity was assessed using the EPDS,²⁰ which is a 10-item self-report measure that omits depressive symptoms that can be conflated with normal pregnancy symptoms. It is frequently used to assess depressive symptom severity during pregnancy.²⁶ Total scores range from 0 to 30, with higher scores indicating greater symptom severity. Scores of 10 or greater suggest minor depression, and scores of 15 or greater suggest major depression among pregnant women.²⁶ Anxiety symptom severity was assessed using the Generalized Anxiety Disorder Scale-7.²⁷ Scores range from 0 to 21, with higher scores indicating greater anxiety symptom severity. Scores of 0 to 4 suggest minimal anxiety, 5 to 9 mild anxiety, 10 to 14 moderate anxiety, and 11 to 21 severe anxiety.

All study measures were self-reported and data was collected using Qualtrics and Research Electronic Data Capture (REDCap) online survey systems. At each time point, participants were asked about their use of the following aids to improve sleep: (1) sleep medication prescribed by a physician; (2) combination sleep aid and pain reliever; (3) over-the-counter or store-bought sleep aid; (4) alternative therapy or herbal supplement; (5) therapy or counseling; (6) alcohol, beer, or wine; (7) eye mask or ear plugs; and (8) other. Participants were also asked about their use of the following aids to improve mood: (1) antidepressant medication; (2) therapy or counseling; (3) support group; (4) alternative therapy or herbal supplement; and (5) other. Response options were rarely or never, a few nights per month, a few nights per week, and every night or almost every night. We compared the use of nonstudy treatments between groups using χ^2 tests. Owing to small sample sizes, responses were recoded to rarely or never vs a few nights per month or more.

Randomization and Procedures

The randomization sequence was generated by an independent investigator using the Sealed Envelope online randomization program with block sizes of 4, 6, and 8.²⁸ The randomization sequence and block sizes were concealed from study investigators and staff members. Randomization was not stratified by any baseline characteristic. The randomization sequence was stored on an electronic file that was inaccessible to the study investigators or staff members. When a participant completed baseline measures, study staff members requested the allocation assignment from the independent investigator.

Individuals interested in participating in the study completed an electronic consent form that described the screening procedures; they then completed a questionnaire battery to collect demographic information and assess their eligibility for participation. The battery included items to assess psychiatric and sleep disorder history, employment in night-shift work, and regular access to the internet. In addition, the battery included the Berlin Questionnaire²⁹ to assess sleep apnea symptoms and results from the ISI, SCI, and EPDS. Eligible individuals completed a demographic survey, viewed the study consent form, and received instructions to complete the sleep diaries.

For 7 consecutive mornings, participants received email requests to complete an online sleep diary. Participants indicated the time they got in bed, the amount of time it took to fall asleep, the number of awakenings, the duration of awakenings, the final awakening time, and the time they got out of bed. Participants who completed at least 4 diaries were invited to proceed to the orientation session.

The orientation session was conducted by phone. The primary goal of this session was to promote participant retention by discussing the importance of the clinical trial, the required commitments, what to expect if randomized to receive digital CBT-I or standard treatment, the rationale for having a control condition and random assignment, and the consequences of attrition bias.³⁰

Participants completed baseline measures on the Qualtrics online survey system. At completion, study staff members requested the condition assignment from the independent investigator, who generated the randomization sequence. Participants were informed of their condition assignment by phone and email.

Participants completed all study measures at postintervention (ie, 10 weeks after randomization), and all study measures with the exception of sleep diaries at follow-up (ie, 18 weeks after randomization). The change from baseline to postintervention was the primary outcome. Participants were sent \$10 electronic gift cards for completing the baseline assessment and each follow-up assessment.

Information about the effect size used in the sample size calculations is available in eMethods in [Supplement 2](#). We used GPower software to perform an analysis of variance of repeated measures with a within-between interaction, which estimated that a sample of 128 participants was required to have 80% power to detect a small to medium effect size ($d = 0.3$), with $\alpha = .01$ for a within-between

interaction. Participant attrition in web-based CBT-I programs ranges from 4% to 22%.^{8,31,32} However, a meta-analysis of computer-based treatments for depression estimated attrition rates of 38.4% in programs that offer administrative support.³³ We used the higher attrition estimate of 38%, yielding a required sample of 208 participants (104 women per intention-to-treat group).

Statistical Analysis

We compared baseline characteristics between groups using 2-sample *t* tests for continuous variables and χ^2 tests for categorical variables. The objective of the statistical analysis was to assess the within-women rates of change in outcomes during the study, specifically the amount of change per week and the differences in these weekly rates of change between women in the digital CBT-I and standard treatment groups. We assessed whether within-woman changes in sleep and mental health outcomes differed between the digital CBT-I and standard treatment groups using linear mixed-effects models.³⁴ These models included the sleep outcomes (diary-defined sleep efficiency and duration as well as results from the ISI, the SCI, and the Pittsburgh Sleep Quality Index) and mental health outcomes (results from the EPDS and the Generalized Anxiety Disorder Scale-7) as the dependent variables, along with time in weeks, intervention group, and time-by-group interactions as the explanatory variables. The models also included random intercepts to accommodate the correlation among the repeated responses within women.

The regression coefficients of time-by-group interactions measure the differences in the rate of within-woman change in the outcomes between the 2 intervention groups. We assessed the statistical significance of the time-by-group interaction using likelihood ratio χ^2 tests, with statistical significance set at $P = .05$. We fit the mixed models using routines in Stata software (StataCorp). The primary analysis assessed differences in changes in insomnia symptom severity from baseline to postintervention, with time measured in weeks. Secondary analyses of additional sleep and mental health outcomes used the same time scale. In addition, we examined change from baseline to follow-up. For a sensitivity analysis, we fit mixed models that used a categorical indicator of time point, as opposed to a continuous measure of time. More details are available in the eMethods, eResults, and eTable in the [Supplement](#). Data were analyzed between December 12, 2018, and July 2, 2019.

In addition to performing statistical tests, we assessed the magnitude of differences in within-woman change between groups using 95% CIs for the time-by-group interaction effect, and we calculated Cohen *d* effect sizes by dividing the between-group postintervention (or follow-up) differences by the baseline pooled SD for continuous outcomes. The absolute Cohen *d* values of 0.2, 0.5, and 0.8 corresponded with small, medium, and large effect sizes. For binary outcomes (eg, insomnia caseness), estimated odds ratios were used as a standard measure of association magnitude.

Results

Participant Enrollment and Characteristics

Of the 2258 women assessed for eligibility using an online self-report questionnaire, 1762 did not meet the eligibility criteria. The 3 most common reasons for ineligibility were (1) the woman was more than 28 weeks pregnant ($n = 463$); (2) the woman did not meet the criteria for an insomnia case or have elevated insomnia symptoms ($n = 371$); and (3) after the modification to the eligibility criteria, the woman did not identify her race as black ($n = 488$). Among the 96 women who declined to participate, the most common reason was noncompletion of the study consent form for unknown reasons after completion of the screening procedures ($n = 85$). Among the 192 participants who were excluded for other reasons, most did not complete at least 4 of 7 daily sleep logs ($n = 85$; [Figure](#)).

The final sample comprised 208 pregnant women, with a mean (SD) age of 33.6 (3.7) years and a mean (SD) gestational age of 17.6 (6.3) weeks at baseline. Most of the participants were white (138 women [66.3%]), married or cohabiting (196 women [94.2%]), had a college degree (180 women [86.5%]), and earned \$100 000 or more per year (141 women [67.8%]). [Table 1](#) presents baseline demographic and clinical characteristics by condition. Information about baseline differences is available in eResults in [Supplement 2](#). Of the 105 participants who were randomized to receive digital CBT-I, 68 women (64.8%) completed all 6 of the sessions, taking a mean (SD) period of 7.97 (2.08) weeks to complete the 6 sessions. A total of 33 women (31.4%) returned to the program for refresher sessions after completing the initial 6 sessions. Seven women (6.7%) never logged in to the digital CBT-I program for unknown reasons. Among the 30 women (28.6%) who started but did not complete the program, the reasons for noncompletion were unknown (21 women [70%]), experienced a miscarriage (3 women [10%]), decided the program was not a good fit for their needs (4 women [13.3%]), started taking an antihistamine medication and experienced improvement in symptoms (1 woman [3.3%]), and was unable to make the time commitment (1 woman [3.3%]).

Baseline to Postintervention and Follow-up

[Table 2](#) presents the results of the mixed-effects analysis comparing rates of change from baseline to postintervention in the primary and secondary outcomes between the digital CBT-I and standard treatment groups. Women in the digital CBT-I group had greater reductions in their insomnia symptom severity scores than women in the standard treatment group, with a weekly change in scores of -0.59 compared with -0.23 , respectively (time-by-group interaction, $\chi^2 = 29.8$; difference $= -0.36$; 95% CI, -0.48 to -0.23); the

difference between these rates was statistically significant ($P < .001$), and the magnitude of the effect size was large ($d = -1.03$). Remission rates, defined as ISI scores of 7 or less, were significantly higher among those in the digital CBT-I group (30 women [44.0%]) vs those in the standard treatment group (21 women [22.3%]; $\chi^2_1 = 9.8$; $P = .002$). The secondary sleep outcomes of sleep efficiency, global sleep quality, and insomnia caseness also exhibited statistically significant time-by-group interactions, with greater reductions in the digital CBT-I group than in the standard treatment group. The time-by-group interaction for sleep duration did not achieve statistical significance (0.03 vs 0.002; difference = 0.028 [95% CI, -0.002 to 0.67]; $P = .07$).

Women in the digital CBT-I group had greater reductions in depressive symptom severity and anxiety symptom severity than women in the standard treatment group, and these differences were statistically significant (for depressive symptom severity, -0.22 vs -0.01; difference = -0.21 [95% CI, -0.30 to -0.11]; $P < .001$; for anxiety symptom severity, -0.19 vs -0.002; difference = -0.188 [95% CI, -0.26 to -0.10]; $P < .001$).

[Table 3](#) presents the results of the mixed-effects analysis to compare rates of change from baseline to follow-up between the digital CBT-I and standard treatment groups. Results of the rates of change from baseline to follow-up were consistent with those from baseline to postintervention; statistically significant time-by-group interactions in the primary outcome, insomnia symptom severity, and all of the secondary sleep and mental health outcomes were observed. Remission rates were also significantly higher among women in the digital CBT-I group (38 women [42.7%]) vs the standard treatment group (26 women [28.6%]; $\chi^2_1 = 3.9$; $P = .048$).

Adverse Events

Three participants randomized to receive standard treatment experienced adverse events (1 stillbirth and 2 miscarriages). These events were determined to be unrelated to study participation because participants in the standard treatment group were free to receive the care they would have typically received if they had not participated in the study, and their health care was in no way restricted. These participants received no study intervention and had no study contact between the time they were notified of their condition assignment and the time of the adverse event.

Three participants randomized to receive digital CBT-I experienced adverse events (3 miscarriages in the first trimester). These events were determined to be possibly related to study participation. It was impossible to rule out a connection between the adverse event and study participation, although an alternative cause was more likely. Two participants had started the digital CBT-I program and reported improved sleep, and 1 participant experienced a miscarriage before beginning the program.

Use of Nonstudy Treatments

Data regarding the use of nonstudy treatments were available from 183 participants (88%) at postintervention and 178 participants (85.6%) at follow-up. At postintervention, significantly more participants receiving standard treatment compared with CBT-I reported using a sleep medication prescribed by a physician (9 participants [9.6%] vs 2 participants [2.2%], respectively; $\chi^2_1 = 4.3$; $P = .04$) or an alternative therapy or herbal supplement to improve sleep at least a few nights per month (15 participants [16%] vs 5 participants [5.6%], respectively; $\chi^2_1 = 5.0$; $P = .03$). No significant differences were observed in the use of other aids to improve sleep at the postintervention or follow-up time points. No condition differences were found in the use of nonstudy treatments to improve mood at either time point.

Discussion

The primary goal of this study was to evaluate the efficacy of digital CBT-I among pregnant women. We found strong support for our hypothesis that digital CBT-I treatment would be associated with significant improvement in insomnia symptoms compared with standard care. During the 10-week study period, insomnia severity scores decreased more than twice as much for participants randomized to receive digital CBT-I compared with participants randomized to receive standard treatment. In addition, women who received digital CBT-I treatment reported greater reductions in the amount of time they lay awake in bed and greater improvements in global sleep quality. Of note, the benefit of digital CBT-I treatment was maintained approximately 2 months after the postintervention time point. In terms of clinical significance, substantially more women randomized to receive digital CBT-I experienced symptom remission compared with women randomized to receive standard treatment.

Our findings add to an emerging body of research suggesting that CBT-I treatment is an effective nonpharmacological approach for treating insomnia symptoms during pregnancy.[6,35,36](#) Our clinical trial extends this literature to indicate that CBT-I treatment can also be effective for subthreshold insomnia symptoms, which are prevalent during pregnancy.[1](#) Moreover, a digital intervention that women can access at their convenience may be particularly attractive to pregnant women, who experience competing demands on their time and energy.

Although the use of sleep medication was rare in this sample, participants randomized to receive standard treatment were more likely to use prescription medication for sleep at the postintervention time point (eResults in [Supplement 2](#)). A paucity of research is available using randomized clinical trials to evaluate the efficacy and safety of pharmacotherapy for insomnia during pregnancy, but

observational studies suggest risks for adverse birth outcomes. Medications frequently prescribed for insomnia in the general population, such as benzodiazepines and zolpidem, are associated with an increased risk of spontaneous abortion, low birth weight, preterm birth, small size for gestational age, and cesarean delivery.^{37,38} Pregnant women prefer nonpharmacological treatments for insomnia,³⁹ and our research indicates that digital CBT-I treatment is an effective and safe intervention for reducing insomnia symptoms.

A secondary goal of this study was to evaluate the efficacy of digital CBT-I treatment for depressive and anxiety symptoms among pregnant women. We found that participants randomized to receive digital CBT-I experienced significantly greater improvements in subclinical depressive and anxiety symptom severity compared with participants randomized to receive standard treatment. Participants entered this study with mild depressive and anxiety symptoms, and it seems that research is needed to evaluate whether CBT-I is effective for treating or preventing perinatal depression or anxiety in those with elevated symptom severity. It is possible that a treatment that improves depressive and anxiety symptoms indirectly may be a less stigmatized entry point for improving perinatal mental health.

We believe this study revealed that pregnant women are highly interested in an intervention that may improve sleep; more than 2000 women completed the eligibility survey. However, one of the most common reasons women were ineligible to participate was that they did not meet the threshold for clinically significant insomnia symptoms. It is important that future research examines interventions to improve less severe sleep disturbances given their high prevalence¹ and consequences.^{11,40,41,42,43,44,45,46} Although more women randomized to receive digital CBT-I experienced remission in insomnia symptoms compared with those randomized to receive standard treatment, most women continued to experience at least subthreshold symptoms. We feel future research should examine whether targeting pregnancy-specific sleep disturbances, such as nocturia and discomfort, helps more women achieve symptom remission. Mindfulness-based and acceptance-based approaches that focus on increasing acceptance of physical symptoms that may be difficult to eliminate may be particularly well suited for pregnancy-related poor sleep.

Limitations

The study had several limitations. First, because we were interested in investigating a scalable intervention format, insomnia outcomes were based on self-reported symptom severity rather than a clinical diagnostic interview. Second, we did not use objective sleep measures because insomnia diagnosis is determined by subjective report of symptoms rather than by objective measures (eg, behavioral assessment using wrist actigraphy).⁴⁷ Third, we did not use an active control comparator group because our primary research question was whether digital CBT-I treatment outperformed a clinically relevant comparator. Finally, the sample was predominantly wealthy, white, and highly educated; future research should examine whether the current findings can be generalized to more diverse populations, who may be disproportionately affected by poor sleep.⁴⁸

Conclusions

To our knowledge, this study was the first randomized clinical trial of digital CBT-I treatment in pregnancy. We found that CBT-I treatment was effective for improving insomnia as well as subclinical anxiety and depressive symptoms. Given the widespread nature of insomnia in pregnancy, the scalability of this intervention, its low-risk profile, and its demonstrated efficacy, digital CBT-I has great promise as a treatment for insomnia in pregnant women.

Notes

Supplement 1.

Trial Protocol

Supplement 2.

eMethods. Changes to Eligibility Criteria, Use of Nonstudy Treatments, Sample Size Considerations, and Statistical Analysis

eResults. Analysis Adjusting for Primiparity, Sensitivity Analysis, and Use of Nonstudy Treatments

eTable. Sensitivity Analysis Results of Linear Mixed-Effects Analysis to Assess Categorical Time (Baseline to Postintervention) by Group (Digital CBT-I vs Standard Treatment) Interaction

Supplement 3.

Data Sharing Statement

References

1. Mindell JA, Cook RA, Nikolovski J. Sleep patterns and sleep disturbances across pregnancy. *Sleep Med.* 2015;16(4):483-488. doi: 10.1016/j.sleep.2014.12.006 [PubMed: 25666847] [CrossRef: 10.1016/j.sleep.2014.12.006]
2. Felder JN, Baer RJ, Rand L, Jelliffe-Pawlowski LL, Prather AA. Sleep disorder diagnosis during pregnancy and risk of preterm birth. *Obstet Gynecol.* 2017;130(3):573-581. doi: 10.1097/AOG.0000000000002132 [PubMed: 28796676] [CrossRef: 10.1097/AOG.0000000000002132]
3. 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. doi: 10.1111/jsr.12858 [PubMed: 30983027] [CrossRef: 10.1111/jsr.12858]
4. Trauer JM, Qian MY, Doyle JS, Rajaratnam SM, Cunnington D. Cognitive behavioral therapy for chronic insomnia: a systematic review and meta-analysis. *Ann Intern Med.* 2015;163(3):191-204. doi: 10.7326/M14-2841 [PubMed: 26054060] [CrossRef: 10.7326/M14-2841]
5. Qaseem A, Kansagara D, Forciea MA, Cooke M, Denberg TD; Clinical Guidelines Committee of the American College of Physicians . Management of chronic insomnia disorder in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2016;165(2):125-133. doi: 10.7326/M15-2175 [PubMed: 27136449] [CrossRef: 10.7326/M15-2175]
6. Manber R, Bei B, Simpson N, et al.. Cognitive behavioral therapy for prenatal insomnia: a randomized controlled trial. *Obstet Gynecol.* 2019;133(5):911-919. doi: 10.1097/AOG.0000000000003216 [PMCID: PMC6485299] [PubMed: 30969203] [CrossRef: 10.1097/AOG.0000000000003216]
7. Thomas A, Grandner M, Nowakowski S, Nesom G, Corbitt C, Perlis ML. Where are the behavioral sleep medicine providers and where are they needed? a geographic assessment. *Behav Sleep Med.* 2016;14(6):687-698. doi: 10.1080/15402002.2016.1173551 [PMCID: PMC5070478] [PubMed: 27159249] [CrossRef: 10.1080/15402002.2016.1173551]
8. Espie CA, Kyle SD, Williams C, et al.. A randomized, placebo-controlled trial of online cognitive behavioral therapy for chronic insomnia disorder delivered via an automated media-rich web application. *Sleep.* 2012;35(6):769-781. doi: 10.5665/sleep.1872 [PMCID: PMC3353040] [PubMed: 22654196] [CrossRef: 10.5665/sleep.1872]
9. Ritterband LM, Thorndike FP, Ingersoll KS, et al.. Effect of a web-based cognitive behavior therapy for insomnia intervention with 1-year follow-up: a randomized clinical trial. *JAMA Psychiatry.* 2017;74(1):68-75. doi: 10.1001/jamapsychiatry.2016.3249 [PubMed: 27902836] [CrossRef: 10.1001/jamapsychiatry.2016.3249]
10. Flynn HA, Henshaw E, O'Mahen H, Forman J. Patient perspectives on improving the depression referral processes in obstetrics settings: a qualitative study. *Gen Hosp Psychiatry.* 2010;32(1):9-16. doi: 10.1016/j.genhosppsych.2009.07.005 [PMCID: PMC2818112] [PubMed: 20114123] [CrossRef: 10.1016/j.genhosppsych.2009.07.005]
11. Skouteris H, Germano C, Wertheim EH, Paxton SJ, Milgrom J. Sleep quality and depression during pregnancy: a prospective study. *J Sleep Res.* 2008;17(2):217-220. doi: 10.1111/j.1365-2869.2008.00655.x [PubMed: 18482110] [CrossRef: 10.1111/j.1365-2869.2008.00655.x]
12. Skouteris H, Wertheim EH, Germano C, Paxton SJ, Milgrom J. Assessing sleep during pregnancy: a study across two time points examining the Pittsburgh Sleep Quality Index and associations with depressive symptoms. *Womens Health Issues.* 2009;19(1):45-51. doi: 10.1016/j.whi.2008.10.004 [PubMed: 19111787] [CrossRef: 10.1016/j.whi.2008.10.004]
13. Osnes RS, Roaldset JO, Follestad T, Eberhard-Gran M. Insomnia late in pregnancy is associated with perinatal anxiety: a longitudinal cohort study. *J Affect Disord.* 2019;248:155-165. doi: 10.1016/j.jad.2019.01.027 [PubMed: 30735852] [CrossRef: 10.1016/j.jad.2019.01.027]
14. Christensen H, Batterham PJ, Gosling JA, et al.. Effectiveness of an online insomnia program (SHUTi) for prevention of depressive episodes (the GoodNight Study): a randomised controlled trial. *Lancet Psychiatry.* 2016;3(4):333-341. doi: 10.1016/S2215-0366(15)00536-2 [PubMed: 26827250] [CrossRef: 10.1016/S2215-0366(15)00536-2]
15. Ye YY, Zhang YF, Chen J, et al.. Internet-based cognitive behavioral therapy for insomnia (ICBT-i) improves comorbid anxiety and depression—a meta-analysis of randomized controlled trials. *PLoS One.* 2015;10(11):e0142258. doi: 10.1371/journal.pone.0142258 [PMCID: PMC4651423] [PubMed: 26581107] [CrossRef: 10.1371/journal.pone.0142258]
16. Espie CA, Kyle SD, Hames P, Gardani M, Fleming L, Cape J. The Sleep Condition Indicator: a clinical screening tool to evaluate insomnia disorder. *BMJ Open.* 2014;4(3):e004183. doi: 10.1136/bmjopen-2013-004183 [PMCID: PMC3964344] [PubMed: 24643168] [CrossRef: 10.1136/bmjopen-2013-004183]
17. Espie CA, Farias Machado P, Carl JR, et al.. The Sleep Condition Indicator: reference values derived from a sample of 200 000 adults. *J Sleep Res.* 2018;27(3):e12643. doi: 10.1111/jsr.12643 [PubMed: 29193493] [CrossRef: 10.1111/jsr.12643]
18. Morin CM. *Insomnia: Psychological Assessment and Management.* New York: Guilford Press; 1993.
19. Bastien CH, Vallieres A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Med.* 2001;2(4):297-307. doi: 10.1016/S1389-9457(00)00065-4 [PubMed: 11438246] [CrossRef: 10.1016/S1389-9457(00)00065-4]
20. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry.* 1987;150:782-786. doi: 10.1192/bjp.150.6.782 [PubMed: 3651732] [CrossRef: 10.1192/bjp.150.6.782]

21. Espie CA, Emsley R, Kyle SD, et al.. Effect of digital cognitive behavioral therapy for insomnia on health, psychological well-being, and sleep-related quality of life: a randomized clinical trial. *JAMA Psychiatry*. 2019;76(1):21-30. doi: 10.1001/jamapsychiatry.2018.2745 [PMCID: PMC6583463] [PubMed: 30264137] [CrossRef: 10.1001/jamapsychiatry.2018.2745]
22. Morin CM, Espie CA. *Insomnia: A Clinical Guide to Assessment and Treatment*. New York: Kluwer Academic/Plenum Publishers; 2003.
23. Morin CM, Belleville G, Belanger L, Ivers H. The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep*. 2011;34(5):601-608. doi: 10.1093/sleep/34.5.601 [PMCID: PMC3079939] [PubMed: 21532953] [CrossRef: 10.1093/sleep/34.5.601]
24. Buysse DJ, Reynolds CF III, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28(2):193-213. doi: 10.1016/0165-1781(89)90047-4 [PubMed: 2748771] [CrossRef: 10.1016/0165-1781(89)90047-4]
25. Espie CA, Kyle SD, Hames P, Cyhlarova E, Benzeval M. The daytime impact of DSM-5 insomnia disorder: comparative analysis of insomnia subtypes from the Great British Sleep Survey. *J Clin Psychiatry*. 2012;73(12):e1478-e1484. doi: 10.4088/JCP.12m07954 [PubMed: 23290331] [CrossRef: 10.4088/JCP.12m07954]
26. Matthey S, Henshaw C, Elliott S, Barnett B. Variability in use of cut-off scores and formats on the Edinburgh Postnatal Depression Scale: implications for clinical and research practice. *Arch Womens Ment Health*. 2006;9(6):309-315. doi: 10.1007/s00737-006-0152-x [PubMed: 17013761] [CrossRef: 10.1007/s00737-006-0152-x]
27. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097. doi: 10.1001/archinte.166.10.1092 [PubMed: 16717171] [CrossRef: 10.1001/archinte.166.10.1092]
28. Create a blocked randomisation list. Version 1.19.0. Sealed Envelope [database online]. <https://www.sealedenvelope.com/simple-randomiser/v1/lists>. Published 2019. Accessed November 6, 2019.
29. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med*. 1999;131(7):485-491. doi: 10.7326/0003-4819-131-7-199910050-00002 [PubMed: 10507956] [CrossRef: 10.7326/0003-4819-131-7-199910050-00002]
30. Goldberg JH, Kiernan M. Innovative techniques to address retention in a behavioral weight-loss trial. *Health Educ Res*. 2005;20(4):439-447. doi: 10.1093/her/cyg139 [PubMed: 15598664] [CrossRef: 10.1093/her/cyg139]
31. Ritterband LM, Thorndike FP, Gonder-Frederick LA, et al.. Efficacy of an internet-based behavioral intervention for adults with insomnia. *Arch Gen Psychiatry*. 2009;66(7):692-698. doi: 10.1001/archgenpsychiatry.2009.66 [PMCID: PMC3723339] [PubMed: 19581560] [CrossRef: 10.1001/archgenpsychiatry.2009.66]
32. Thorndike FP, Ritterband LM, Gonder-Frederick LA, Lord HR, Ingersoll KS, Morin CM. A randomized controlled trial of an internet intervention for adults with insomnia: effects on comorbid psychological and fatigue symptoms. *J Clin Psychol*. 2013;69(10):1078-1093. doi: 10.1002/jclp.22032 [PMCID: PMC4078738] [PubMed: 24014057] [CrossRef: 10.1002/jclp.22032]
33. Richards D, Richardson T. Computer-based psychological treatments for depression: a systematic review and meta-analysis. *Clin Psychol Rev*. 2012;32(4):329-342. doi: 10.1016/j.cpr.2012.02.004 [PubMed: 22466510] [CrossRef: 10.1016/j.cpr.2012.02.004]
34. McCulloch CE, Searle SR, Neuhaus JM. *Linear and Mixed Models*. 2nd ed New York: Wiley; 2008.
35. Tomfohr-Madsen LM, Clayborne ZM, Rouleau CR, Campbell TS. Sleeping for two: an open-pilot study of cognitive behavioral therapy for insomnia in pregnancy. *Behav Sleep Med*. 2017;15(5):377-393. doi: 10.1080/15402002.2016.1141769 [PubMed: 27124405] [CrossRef: 10.1080/15402002.2016.1141769]
36. Cain MA, Brumley J, Louis-Jacques A, Drerup M, Stern M, Louis JM. A pilot study of a sleep intervention delivered through group prenatal care to overweight and obese women [published online May 25, 2019]. *Behav Sleep Med*. 2019;1-11. doi: 10.1080/15402002.2019.1613995 [PubMed: 31130005] [CrossRef: 10.1080/15402002.2019.1613995]
37. Wang LH, Lin HC, Lin CC, Chen YH, Lin HC. Increased risk of adverse pregnancy outcomes in women receiving zolpidem during pregnancy. *Clin Pharmacol Ther*. 2010;88(3):369-374. doi: 10.1038/clpt.2010.97 [PubMed: 20686480] [CrossRef: 10.1038/clpt.2010.97]
38. Sheehy O, Zhao JP, Berard A. Association between incident exposure to benzodiazepines in early pregnancy and risk of spontaneous abortion. *JAMA Psychiatry*. 2019;76(9):848-957. doi: 10.1001/jamapsychiatry.2019.0963 [PMCID: PMC6537838] [PubMed: 31090881] [CrossRef: 10.1001/jamapsychiatry.2019.0963]
39. Sedov ID, Goodman SH, Tomfohr-Madsen LM. Insomnia treatment preferences during pregnancy. *J Obstet Gynecol Neonatal Nurs*. 2017;46(3):e95-e104. doi: 10.1016/j.jogn.2017.01.005 [PubMed: 28343943] [CrossRef: 10.1016/j.jogn.2017.01.005]
40. Baglioni C, Battagliese G, Feige B, et al.. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. *J Affect Disord*. 2011;135(1-3):10-19. doi: 10.1016/j.jad.2011.01.011 [PubMed: 21300408] [CrossRef: 10.1016/j.jad.2011.01.011]
41. Gelaye B, Addae G, Neway B, et al.. Poor sleep quality, antepartum depression and suicidal ideation among pregnant women. *J Affect Disord*. 2017;209:195-200. doi: 10.1016/j.jad.2016.11.020 [PMCID: PMC5360461] [PubMed: 27930912] [CrossRef: 10.1016/j.jad.2016.11.020]
42. Cai S, Tan S, Gluckman PD, et al.; GUSTO study group . Sleep quality and nocturnal sleep duration in pregnancy and risk of gestational diabetes mellitus. *Sleep*. 2017;40(2):zsw058. doi: 10.1093/sleep/zsw058 [PubMed: 28364489] [CrossRef: 10.1093/sleep/zsw058]
43. Blair LM, Porter K, Leblebicioglu B, Christian LM. Poor sleep quality and associated inflammation predict preterm birth: heightened risk among African Americans. *Sleep*. 2015;38(8):1259-1267. doi: 10.5665/sleep.4904 [PMCID: PMC4507731] [PubMed: 25845693] [CrossRef: 10.5665/sleep.4904]

44. Okun ML, Schetter CD, Glynn LM. Poor sleep quality is associated with preterm birth. *Sleep*. 2011;34(11):1493-1498. doi: 10.5665/sleep.1384 [PMCID: PMC3198204] [PubMed: 22043120] [CrossRef: 10.5665/sleep.1384]
45. Li R, Zhang J, Zhou R, et al.. Sleep disturbances during pregnancy are associated with cesarean delivery and preterm birth. *J Matern Fetal Neonatal Med.* 2017;30(6):733-738. doi: 10.1080/14767058.2016.1183637 [PubMed: 27125889] [CrossRef: 10.1080/14767058.2016.1183637]
46. Lee KA, Gay CL. Sleep in late pregnancy predicts length of labor and type of delivery. *Am J Obstet Gynecol.* 2004;191(6):2041-2046. doi: 10.1016/j.ajog.2004.05.086 [PubMed: 15592289] [CrossRef: 10.1016/j.ajog.2004.05.086]
47. American Psychiatric Association *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed Washington, DC: American Psychiatric Association; 2013.
48. Amyx M, Xiong X, Xie Y, Buckens P. Racial/ethnic differences in sleep disorders and reporting of trouble sleeping among women of childbearing age in the United States. *Matern Child Health J.* 2017;21(2):306-314. doi: 10.1007/s10995-016-2115-9 [PMCID: PMC5250592] [PubMed: 27439422] [CrossRef: 10.1007/s10995-016-2115-9]

Figures and Tables

Figure.

CONSORT Diagram

Table 1.

Participant Baseline Demographic and Clinical Characteristics by Condition

Abbreviation: CBT-I, cognitive behavioral therapy for insomnia.

^aThe t_{206} statistic.

^bThe χ^2_1 statistic.

^cMeasured by the Insomnia Severity Index.

^dMeasured by sleep diary.

^eMeasured by the Pittsburgh Sleep Quality Index.

^fMeasured by the Sleep Condition Indicator.

^gMeasured by the Edinburgh Postnatal Depression Scale.

^hMeasured by the Generalized Anxiety Disorder Scale-7.

Table 2.

Linear Mixed-Effects Analysis of Change From Baseline to Postintervention by Group Interaction

Abbreviations: CBT-I, cognitive behavioral therapy for insomnia; NA, not applicable.

^aChange is per week from baseline to postintervention.

^bThe χ^2 is from a likelihood ratio test.

Table 3.

Linear Mixed-Effects Analysis of Change From Baseline to Follow-Up by Group Interaction

Abbreviations: CBT-I, cognitive behavioral therapy for insomnia; NA, not applicable.

^aChange is per week from baseline to follow-up.

^bThe χ^2 is from a likelihood ratio test.