Date: Dec 11, 2018
To: "Rachel Manber" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-18-2049

RE: Manuscript Number ONG-18-2049

Cognitive Behavioral Therapy for Prenatal Insomnia: A Randomized Controlled Trial

Dear Dr. Manber:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jan 01, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1:

This is an extremely well-written report that describes a clinical trial of CBTI (cognitive behavioral therapy for insomnia) in pregnant women. CBTCI was compared to a control therapy. The authors explain the rationale for the study. It would be nice if, in the introduction, they mention prior work with this treatment in pregnant women and other populations. Pregnant women are well known to have sleeping difficulties, especially toward the end of pregnancy, and this intervention may be a non-pharmacological management approach.

All components of CONSORT are included.

My only other comment is that it would be nice to have information on the accessibility of the treatment. For example, there is a computerized version that is available, although not tested in pregnant women, they would make the intervention accessible to practitioners. This also would enhance the clinical significance of the findings reported herein.

Reviewer #2:

1. Abstract.
a. The methods might include something about each therapy. An Ob/Gyn readership is not likely to understand what active control therapy entails. Might also mention the inclusion criteria.
b. Insomnia remission is in the results but not the methods.
c. The conclusion is that CBTI is an effective "alternative to pharmacological treatments," but the authors did not study pharmacological treatment.

2. Introduction.
a. The authors are introducing a topic that is of interest to the readership and to our patients but is not generally treated by an Ob/Gyn. Therefore, it would be helpful to include more factual content, with relevant percentages and definitions. Might include something about the insomnia severity index and why it was selected for the primary outcome.
b. Lines 60-64. These are not generally considered unique risks. Neither SGA nor LGA is an adverse outcome (each is the 10th percentile). The authors might want to phrase this section differently, e.g. reasons why pregnant women have trouble sleeping and when this constitutes severe insomnia.
c. Rather than explaining that the AASM does not recommend sedative hypnotics, might educate us about different types of non-pharmacologic options.

3. Methods. This section is very well written and is clearly presented.
a. Women were recruited from prenatal clinics. Were all women receiving prenatal care screened for insomnia? From Figure 1, more that 250 women completed screening, but only 23 did not meet criteria for severe insomnia. Readers will probably be curious about the proportion of women receiving prenatal care who met criteria for having severe insomnia.
b. Why 18-32 weeks? This spans early 2nd trimester to mid-third. Suggest adjusting for trimester or stratifying. Also, why was the minimal duration of insomnia modified from 3 months to 1 month?
c. Line 97. Would include something about the DSM criteria (readership is unlikely to be familiar with this).
d. What kind of unstable medical conditions (line 98)?
e. Lines 151-153. When the authors write that the CTRL therapy produces low response rates, do they mean it doesn't work well? Is that consistent with the 52% response rate that the authors found?
f. Why was a postnatal depression scale tested in prenatal patients? Would include a sentence about the rationale for using this in women without depression. Has this been validated?

4. Results.
a. Tables. Please provide the N's at the top of the table columns. Please make sure the number of significant digits is clinically relevant, e.g. age can be expressed in years.
b. Table 1. A more typical order and content would be to start with age, then race/ethnicity, then parity (nulliparous, multiparous).
The reader will need information as to how to interpret the ISI and EPDS results. This might be provided as couple of sentences in the results text. Might the significant difference in EDPS score be related to success of treatment in this group (improvement in depressive symptoms resulting in improved insomnia)?
If group differences were tested using Fisher's exact test (rather than chi-square), then why are p-values presented for chi-square analyses?
c. Table 2. The total wake time after therapy was 48 minutes in the CBTI group and 87 minutes in the control group. That wasn't statistically significant?

5. Discussion.
a. Line 252. If reporting 64%, would include the percentage of the control group as well (52%) and would address the high response rate among controls.
b. Line 256. Not really necessary to call it suffering in a vulnerable population (considering other adverse outcomes in our field).
c. Lines 271-281. Generalizability of findings may be related to availability and to cost and coverage of therapy. Might mention something about these topics.
d. In the concluding paragraph, the authors write that their study extends the findings from another study (references 40 and 41) that supports CBTI as effective treatment for insomnia during pregnancy. Suggest including these studies earlier in the discussion, and probably in greater detail.

Reviewer #3: Insomnia is a distressing and potentially damaging symptom for pregnant and postpartum women, and the avoidance of pharmacological treatment is highly desirable. This study was carefully planned, executed, and described. My concerns are essentially about the discussion. First of all, the lack of change in objective wakefulness, while not a new finding, is noteworthy. Was the difference between the two therapies really due to the specifics of the study intervention, or to a perceived difference in psychological support and intensity? Secondly, how likely is it that pregnant patients can access either modality, since most have jobs and/or children to care for during the day, and few obstetrical care settings(and health insurance plans) are likely to offer the new(or any) insomnia treatment.

STATISTICAL EDITORS' COMMENTS:

1. lines 39-42: Was there sufficient counts in each strata (Hispanic vs non-Hispanic; English or Spanish language; GA at treatment) to have sufficient power to discern a difference? It seems the primary was based on all, not subsets, so the NS findings cannot be generalized.

2. lines 33-34, Fig 2, lines 290-293: Might the maternal insomnia be a function of GA? The entry GA of 18-32 weeks comprises a wide range and should have randomized by blocks of GA. This is especially important since the control group had (fig 2) a drop in ISI scores over time, although not as much as the treatment group, so clearly there was a temporal change independent of the CBTI.

3. lines 201-202: Were the 254 women all eligible, and if not, what were the reasons for exclusion. Should include a flow diagram to explain how 254 screened became 194, then 179 analyzed and how many in each treatment group.

4. line 229: The survival curve analysis is in Figure 3, which depicts non-remission, not ISI scores.

5. lines 283-286: This is unfortunate. The randomization process should have occurred closer in time to the baseline and initiation of treatment. What were the demographic/clinical characteristics of the 15 who dropped out and which treatment group were they assigned?

6. Table 1: Since this is an RCT, it is not necessary to include stats comparisons of baseline characteristics. However, the analysis presented does not include comparison of GA at entry, which should be enumerated.

7. Table 2: Need to clearly separate the primary (ISI) from the secondary outcomes.

8. Fig 2: Were these lines derived from the data or a model? The endpoints at 50 days do not correspond to Table 2 post values of 8.03 and 11.19.

9.Fig 3: Need to include the number remaining at the time points along the x-axis.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

2. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. This statement must appear at the end of your Materials and Methods section. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Examples of statements can be found online at http://www.icmje.org/news-and-editorials/data_sharing_june_2017.pdf.

3. Based on the forms that have been submitted, Dr. Anita Sit has not met the criteria for authorship. On the third page of the form, under the section labeled "Authorship," items #2-4, in addition to either 1a or 1b, must be checked off in order to qualify for authorship. Dr. Sit should be moved to the acknowledgments, or they could resubmit a revised author agreement form if they filled it out erroneously the first time. All updated and missing forms should be uploaded with the revision in Editorial Manager.

4. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendixes).

Please limit your Introduction to 250 words and your Discussion to 750 words.

6. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

* All financial support of the study must be acknowledged.
* Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
* All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your signature on the journal's author agreement form verifies that permission has been obtained from all named persons.
* If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

7. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

8. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Original Research articles, 300 words. Please provide a word count.

9. Only standard abbreviations and acronyms are allowed. A selected list is available online at http://edmgr.ovid.com /ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

10. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

11. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

12. The Journal's Production Editor has the following comments on the figures in your manuscript:

"Figure 3: Is this available in color? "

When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file).

If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Figures should be no smaller than the journal column size of 3 1/4 inches. Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. Refer to the journal printer's web site (http://cjs.cadmus.com/da/index.asp) for more direction on digital art preparation.

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If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors, that each author has given approval to the final form of the revision, and that the agreement form signed by each author and submitted with the initial version remains valid.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jan 01, 2019, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

The Editors of Obstetrics & Gynecology

2017 IMPACT FACTOR: 4.982
2017 IMPACT FACTOR RANKING: 5th out of 82 ob/gyn journals

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Editors,
Obstetric and Gynecology

1/14/2019

RE: Manuscript Number ONG-18-2049

This is a re-submission of the revised manuscript entitled “Cognitive Behavioral Therapy for Prenatal Insomnia: A Randomized Controlled Trial” to *Obstetrics & Gynecology*.

We appreciate the careful review and the opportunity to revise and resubmit. We have tracked changes whenever addressing a comment and also reference the line number where each point is addressed. However, we did not track additional edits that were made purely for condensing the text of the introduction and discussion to conform to the word count requirement. Please see below my signature point by point response to all the comments by the reviewers and the editorial board.

Word counts:
Abstract: 284 words
Introduction: 250 words
Discussion: 745 words
Total: 5,133 words, 22 pages

Rachel Manber, PhD
Professor
Department of Psychiatry & Behavioral Sciences
Director, Stanford Sleep Health & Insomnia Program
Stanford University School of Medicine

RESPONSE TO REVIEWERS AND EDITORIAL BORAD COMMENTS

Reviewer #1

This is an extremely well-written report that describes a clinical trial of CBTI (cognitive behavioral therapy for insomnia) in pregnant women. CBTI was compared to a control therapy. The authors explain the rationale for the study.

1. It would be nice if, in the introduction, they mention prior work with this treatment in pregnant women and other populations. Pregnant women are well known to have sleeping difficulties, especially toward the end of pregnancy, and this intervention may be a non-pharmacological management approach.

   RESPONSE: Regarding prior work on CBTI in non-pregnant populations, we now explicitly state that CBTI has strong empirical support (lines 65). Regarding prior work on CBTI during pregnancy, we moved the mention of two studies of CBTI-based approaches during pregnancy from the discussion to the introduction (lines 69-71). We note that there were no published studies about CBTI in pregnant women when we began our study. These two small studies were published in the past two years and neither was an RCT.
   One of these two studies was a single arm evaluation of group CBTI; it found a significant pre- to post-treatment decrease in ISI among 13 treatment completers [1]. The other study evaluated a self-help version of CBTI using a quasi-experimental design; it found no significant effect of the intervention during pregnancy among 24 treatment completers [2].

2. All components of CONSORT are included.

   RESPONSE: NA

3. It would be nice to have information on the accessibility of the treatment. For example, there is a computerized version that is available, although not tested in pregnant women, they would make the intervention accessible to practitioners. This also would enhance the clinical significance of the findings reported herein.

   RESPONSE: We agree and added to the last paragraph a brief discussion of access to care, including availability of internet based CBTI (lines 341-344).

Reviewer #2:

1. <u>Abstract.</u>

a. The methods might include something about each therapy. An Ob/Gyn readership is not likely to understand what active control therapy entails. Might also mention the inclusion criteria.

   RESPONSE: We added to the abstract details about the interventions (lines 34-37). We moved inclusion criteria from the results to the method section of the abstract and added exclusion criteria (lines 32-34).

b. Insomnia remission is in the results but not the methods.

RESPONSE: We added the definition of insomnia remission to the methods section of the abstract (line 30).

We also moved the definition from the results to the methods section of the manuscript (line 175).

c. The conclusion is that CBTI is an effective "alternative to pharmacological treatments," but the authors did not study pharmacological treatment.

RESPONSE: We replaced the text: “alternative to pharmacological treatments“ with the text: “non-pharmacological treatment“ (line 49).

2. Introduction.

a. The authors are introducing a topic that is of interest to the readership and to our patients but is not generally treated by an Ob/Gyn. Therefore, it would be helpful to include more factual content, with relevant percentages and definitions. Might include something about the insomnia severity index and why it was selected for the primary outcome.

RESPONSE: We added information about why the ISI was selected for the primary outcome (lines 75). We also added prevalence information (lines 59-60).

b. Lines 60-64. These are not generally considered unique risks. Neither SGA nor LGA is an adverse outcome (each is the 10th percentile). The authors might want to phrase this section differently, e.g. reasons why pregnant women have trouble sleeping and when this constitutes severe insomnia.

RESPONSE: We agree and deleted the discussion of negative consequences of poor sleep during pregnancy and added a discussion of reasons why pregnant women have trouble sleeping and when this constitutes an insomnia disorder that merits treatment (lines 56-59). To adhere to word limitation (250 words in the introduction) we did not discuss why pregnant women have trouble sleeping, assuming that readership of this journal will be familiar with pregnancy related factors that impact sleep, which include physical discomfort, fetal movement, and nocturia. Some of these factors were already mentioned in the discussion section.

c. Rather than explaining that the AASM does not recommend sedative hypnotics, might educate us about different types of non-pharmacologic options.

RESPONSE: We removed the sentence about AASM recommendations. Given the word limitation of the introduction section (250 words) we maintained our focus on CBTI and did not add a discussion of other non-pharmacological therapies for insomnia. We note here that there are a few studies of mind-body treatments, such as Tai Chi, yoga, and acupuncture, for insomnia in the general population but empirical support for these interventions is not strong [3].

3. Methods. This section is very well written and is clearly presented.

a. Women were recruited from prenatal clinics. Were all women receiving prenatal care screened for insomnia? From Figure 1, more that 250 women completed screening, but only 23 did not meet criteria for severe insomnia. Readers will probably be curious about the proportion of women receiving prenatal care who met criteria for having severe insomnia.

RESPONSE: We did not systematically screen all women receiving prenatal care for insomnia. Instead we screened only those who were interested in the study, and therefore we cannot

derive estimates of prevalence from our data. Prevalence estimates of insomnia based on past research are explicated in lines 59-60.

b. Why 18-32 weeks? This spans early 2nd trimester to mid-third. Suggest adjusting for trimester or stratifying. Also, why was the minimal duration of insomnia modified from 3 months to 1 month?

RESPONSE:
The lower limit, 18 weeks, was selected for several reasons. It was more efficient to recruit from ultrasound facilities than from prenatal office visits. Therefore, many women were given information about the study during their nuchal translucency ultrasounds at the end of the first trimester, allowing them time to consider study participation. This led to a concern about the possibility of having under-representation of women in the first trimester. The upper limit, 32 weeks, was selected to allow enough time to screen, treat and conduct post treatment assessments before delivery. Finally, we attempted to minimize potentially confounding differences (e.g. nausea/vomiting or physical differences) that may arise at different periods during pregnancy, leading us to choose a time period rather than the entire duration of pregnancy.

As reported in the original submission, we tested a model where we adjusted for gestation week at study entry and found that the results remained the same.
In our original NIH proposal we intended to use the DSM-IV-TR. The DSM-5 was published after we received the NIH award and shortly before we started recruitment. To increase relevance of the findings for the time the results will be obtained, we decided to use to the DSM-5 diagnoses criteria instead. However, we also chose to retain the DSM-IV minimum duration criterion of one month, rather than the DSM-5 minimum duration of three months. This was done in order to broaden the clinical relevance of our findings. We reasoned that it is important to test the intervention in a sample that include women whose clinically significant insomnia emerges during pregnancy, even when the duration of the symptoms was less than three months. This explanation is also included in lines 101-104 of the manuscript.

c. Line 97. Would include something about the DSM criteria (readership is unlikely to be familiar with this).

RESPONSE: We added a description of the essential DSM criteria (lines 95-101).

d. What kind of unstable medical conditions (line 98)?

RESPONSE: The only two uncontrolled medical conditions we ended up excluding for were uncontrolled thyroid or seizure disorders. We revised the text to indicate these two exclusions (lines 105-106).

e. Lines 151-153. When the authors write that the CTRL therapy produces low response rates, do they mean it doesn't work well? Is that consistent with the 52% response rate that the authors found?

RESPONSE: The sentence refers to remission rates in past research which was cited. We changes the term “response rates” to “remission rates” in the text and added the range of remission rates in the studies that were cited in that sentence (lines 161-162). We found much higher remission rates in the current study, which we interpret as a stronger placebo effect during pregnancy and discuss in lines 277-280.

f. Why was a postnatal depression scale tested in prenatal patients? Would include a sentence about the rationale for using this in women without depression. Has this been validated?

RESPONSE: The Edinburgh Postnatal Depression Scale is validated for use during pregnancy. We added this information to the measures section (lines 182-184).

4. Results.

a. Tables. Please provide the N's at the top of the table columns. Please make sure the number of significant digits is clinically relevant, e.g. age can be expressed in years.

RESPONSE: We have adjusted significant digits in the tables and added N values. We did not track these changes.

b. Table 1. A more typical order and content would be to start with age, then race/ethnicity, then parity (nulliparous, multiparous).

RESPONSE: We have revised the order of lines in the table and added parity.

The reader will need information as to how to interpret the ISI and EPDS results. This might be provided as couple of sentences in the results text.

RESPONSE: In the measures section we expanded the information for interpreting the ISI (line 174) and added information about EPDS cutoffs for screening depression during pregnancy (lines 182-184).

Might the significant difference in EDPS score be related to success of treatment in this group (improvement in depressive symptoms resulting in improved insomnia)?

RESPONSE: Although there was a statistically significant decrease in EPDS scores in the full sample, there was little difference in the reduction of EPDS scores between the two treatment arms. This suggests that reduced depression is unlikely to have accounted for differences in improvement in insomnia between the two treatment arms.
We also note that we previously reported that among RCT participants with major depressive disorder and using the same control insomnia therapy, improvement in insomnia following a combination of antidepressant medications and CBTI mediated remission of depression, but not vice versa: improvement in depression did not mediate remission of insomnia [4].

If group differences were tested using Fisher's exact test (rather than chi-square), then why are p-values presented for chi-square analyses?

RESPONSE: Thank you for pointing this out. Following the comment from the statistical editor (comment 6) we deleted the last column (p-values) and all reference to statistical testing from the caption.

c. Table 2. The total wake time after therapy was 48 minutes in the CBTI group and 87 minutes in the control group. That wasn't statistically significant?

RESPONSE: The 48 vs 87 minute figures are for self-reported total wake time values (derived from the sleep diary). We did report in the original manuscript that the CBT-I group had

significantly greater reduction in self-reported total wake time. Our non-significant result pertains to objective total wake time (derived from actigraphy), where the post-treatment values are 95 minutes in each arm.

5. Discussion.

a. Line 252. If reporting 64%, would include the percentage of the control group as well (52%) and would address the high response rate among controls.

RESPONSE: This is an excellent point. We added the CTRL group remission rate and a discussion of the high remission rate observed in our study (lines 277-280).

b. Line 256. Not really necessary to call it suffering in a vulnerable population (considering other adverse outcomes in our field).

RESPONSE: We appreciate the perspective and modified the text accordingly (lines 273-277).

c. Lines 271-281. Generalizability of findings may be related to availability and to cost and coverage of therapy. Might mention something about these topics.

RESPONSE: We agree and added these and other clinically relevant points (lines 341-344).

d. In the concluding paragraph, the authors write that their study extends the findings from another study (references 40 and 41) that supports CBTI as effective treatment for insomnia during pregnancy. Suggest including these studies earlier in the discussion, and probably in greater detail.

RESPONSE: In the response to the first comment by Reviewer 1, the discussion of the two existing uncontrolled studies was moved from the discussion to the introduction. Given word limitation in the introduction (250 words) and the facts that both were very small and neither had a randomized-controlled design, we did not provide additional detail about them in the manuscript. To allow the reviewer to evaluate our decision we briefly described these two studies in our response to the first comment of Reviewer 1.

Reviewer #3:

Insomnia is a distressing and potentially damaging symptom for pregnant and postpartum women, and the avoidance of pharmacological treatment is highly desirable. This study was carefully planned, executed, and described. My concerns are essentially about the discussion.

1. First of all, the lack of change in objective wakefulness, while not a new finding, is noteworthy. Was the difference between the two therapies really due to the specifics of the study intervention, or to a perceived difference in psychological support and intensity?

RESPONSE: We have taken care to equate the non-specific factors mentioned by the reviewer. The two therapies had equal frequency and duration. The therapists in both interventions were trained to respond in a similar manner when a participant raised non-sleep issues, by briefly acknowledging the issue and refocusing the session on sleep. We therefore believe that non-specific factor were most likely equivalent between the two treatments and are not likely to explain the differential effect between the two treatments in subjective outcomes.

2. Secondly, how likely is it that pregnant patients can access either modality, since most have jobs and/or children to care for during the day, and few obstetrical care settings (and health insurance plans) are likely to offer the new (or any) insomnia treatment.

   RESPONSE: We have expanded the last paragraph to include a discussion of access to care. Whereas most health insurance providers cover CBTI as a psychotherapy, there is indeed a shortage of trained therapists. In the last paragraph of the discussion section (lines 341-344) we discuss promising trends in the field that aim to address the access issue.

STATISTICAL EDITORS' COMMENTS:

1. Lines 39-42: Was there sufficient counts in each strata (Hispanic vs non-Hispanic; English or Spanish language; GA at treatment) to have sufficient power to discern a difference? It seems the primary was based on all, not subsets, so the NS findings cannot be generalized.

   RESPONSE: Indeed this study was not designed to have sufficient power to discern difference in these three strata and, therefore, the primary analyses did not include these strata. Analyses pertaining to these three strata were considered exploratory and therefore results should be interpreted cautiously. We removed mention of these factors from the abstract.

2. Lines 33-34, Fig 2, lines 290-293: Might the maternal insomnia be a function of GA? The entry GA of 18-32 weeks comprises a wide range and should have randomized by blocks of GA. This is especially important since the control group had (fig 2) a drop in ISI scores over time, although not as much as the treatment group, so clearly there was a temporal change independent of the CBTI.

   RESPONSE: Although we did not randomize by blocks based on gestational age categories, we did test if adding gestation week to the model changed the results and found that this was not the case. Nonetheless, given that we did not randomize by blocks based on gestational age, we cannot definitely infer that gestational age at study entry does not impact response to treatment.

   We note that, in the absence of treatment, the trajectory of change in insomnia is towards increase rather than decrease in insomnia severity [5]. We interpret the reduction in insomnia severity in the control therapy as likely due to its strong placebo effect and have added this interpretation to the discussion of the high remission rate in the CTRL (line 278-280).

3. Lines 201-202: Were the 254 women all eligible, and if not, what were the reasons for exclusion. Should include a flow diagram to explain how 254 screened became 194, then 179 analyzed and how many in each treatment group.

   RESPONSE: Figure 1 (consort figure) provides these details.

4. Line 229: The survival curve analysis is in Figure 3, which depicts non-remission, not ISI scores.

   RESPONSE: Thank you for spotting this typo. We corrected the text (now line 248) to refer to Figure 3 rather than Figure 2.

5. Lines 283-286: This is unfortunate. The randomization process should have occurred closer in time to the baseline and initiation of treatment. What were the demographic/clinical characteristics of the 15 who dropped out and which treatment group were they assigned?

RESPONSE: The reason randomization occurred earlier than baseline was pragmatic; it allowed time for coordinating treatment initiation (e.g., assigning a study therapist based on participant availability for treatment and language preference, and scheduling of therapy sessions), which was critical given that some women were screened later in pregnancy.

As is depicted in Figure 1 (CONSORT Figure), the number of participants who dropped out before completing baseline measures was 7 in CBTI and 8 in CTRL.

As indicated in lines 220-223, "The 15 participants who discontinued participation before providing baseline data on clinical measures did not differ demographically from participants who were analyzed for testing a priori hypotheses". The table below describes the demographic characteristics of these 15 participants. Note that, given that these participants dropped out before providing ISI (and EPDS) data, we could not conduct a comparison for the clinical data.

Demographics of Recruitment Participants Who Did Not Provide Baseline Data and Excluded from Analyses

N = 15	*Mean* or *n*	*SD* or %
Age (years)	32	6
Nulliparous	6	40%
Race		
White	5	33.3%
Black	3	20%
Asian	2	13.3%
Other	3	20%
Unknown	2	13.3%
Hispanic ethnicity	6	40%
Prefer Spanish	3	20%
Annual family income below $55K	5	33.3%

6. Table 1: Since this is an RCT, it is not necessary to include stats comparisons of baseline characteristics. However, the analysis presented does not include comparison of GA at entry, which should be enumerated.

   RESPONSE: As advised, we deleted from Table 1 the column reporting p-values (Untracked change). We also removed the word "significantly" in the discussion of baseline characteristics (lines 224-225). We note that GA was included in Table 1 in the original submission.

7. Table 2: Need to clearly separate the primary (ISI) from the secondary outcomes.

   RESPONSE: We revised the table to identify the ISI as the primary outcome. This allowed us to address this comment while conforming the journal guidelines to avoid sub-headings.

8. Fig 2: Were these lines derived from the data or a model? The endpoints at 50 days do not correspond to Table 2 post values of 8.03 and 11.19.

   RESPONSE: Figure 2 depicts model estimated trajectories. We revised the legend to specify this. In contrast, the numbers in Table 2 used the last observation available for each participants. Values from Table 2 match numbers that derived from Figure 2 when x-axis is around 36 days, which is the average number of days from baseline to the day on which the final ISI was completed (SD = 11).

9. Fig 3: Need to include the number remaining at the time points along the x-axis.

   RESPONSE: We have now added numbers at risk at the x-axis of Figure 3. We revised Figure 3 legend by adding the following (lines 451-453): "The analysis was based on all participants who provided at least one post-baseline ISI score. Numbers at risk (i.e., non-remission) are displayed under the x-axis."

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter, as well as subsequent author queries. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:
   1. OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries.
   2. OPT-OUT: No, please do not publish my response letter and subsequent email correspondence related to author queries.

   RESPONSE: OPT-IN: Yes, please publish my response letter and subsequent email correspondence related to author queries

2. Clinical trials submitted to the journal as of July 1, 2018, must include a data sharing statement. This statement must appear at the end of your Materials and Methods section. The statement should indicate 1) whether individual deidentified participant data (including data dictionaries) will be shared; 2) what data in particular will be shared; 3) whether additional, related documents will be available (eg, study protocol, statistical analysis plan, etc.); 4) when the data will become available and for how long; and 5) by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Examples of statements can be found online at http://www.icmje.org/news-and-editorials/data_sharing_june_2017.pdf.

   RESPONSE: A data sharing plan was added as the last paragraph of the methods section (lines 186-191).

3. Based on the forms that have been submitted, Dr. Anita Sit has not met the criteria for authorship. On the third page of the form, under the section labeled "Authorship," items #2-4, in addition to either 1a or 1b, must be checked off in order to qualify for authorship. Dr. Sit should be moved to the acknowledgments, or they could resubmit a revised author agreement form if they filled it out erroneously the first time. All updated and missing forms should be uploaded with the revision in Editorial Manager.

   RESPONSE: Dr. Sit has made significant contribution to the data collection. A revised author agreement form is being uploaded.

4. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology will be transitioning as much as possible to use of the reVITALize definitions, and we encourage authors to familiarize themselves with them. The obstetric data definitions are available at http://links.lww.com/AOG/A515, and the gynecology data definitions are available at http://links.lww.com/AOG/A935.

   RESPONSE: We have conformed to the definitions

5. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Original Research reports should not exceed 22 typed, double-spaced pages (5,500 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and appendixes).

   Please limit your Introduction to 250 words and your Discussion to 750 words.

   RESPONSE: We revised the introduction and discussion to address the comments above and edited the original text to conform to these word limits. The introduction is now 251 words and the discussion is 745 words. The manuscript length is 22 pages (5127 words).

6. Specific rules govern the use of acknowledgments in the journal. Please edit your acknowledgments or provide more information in accordance with the following guidelines:

   * All financial support of the study must be acknowledged.
   * Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
   * All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your signature on the journal's author agreement form verifies that permission has been obtained from all named persons.
   * If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

   RESPONSE: All financial support of the study were acknowledged. We did not receive any direct or indirect paid assistance in preparing the manuscript. All the individuals that were acknowledged by name have provided written permission to be acknowledged. Part of the

paper was presented at the annual meeting of the Association of Professional Sleep Societies on June 03, 2018 in Baltimore, Maryland.

7. Provide a short title of no more than 45 characters (40 characters for case reports), including spaces, for use as a running foot.

   RESPONSE: The short title is now 30 characters, including spaces.

8. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

   In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Original Research articles, 300 words. Please provide a word count.

   RESPONSE: We carefully reviewed the abstract to ensure consistency with the rest of the manuscript and that it includes no information that is not in the body of the manuscript, and that the conclusion is clear. The abstract is now 284 words.

9. Only standard abbreviations and acronyms are allowed. A selected list is available online athttp://edmgr.ovid.com/ong/accounts/abbreviations.pdf. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

   RESPONSE: We believe we adhered to this guidelines

10. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

    RESPONSE: We eliminated virgule symbols from the body of the manuscript. This symbol still appears in some references.

11. Please review the journal's Table Checklist to make sure that your tables conform to journal style. The Table Checklist is available online here: http://edmgr.ovid.com/ong/accounts/table_checklist.pdf.

    RESPONSE: We revised the tables to conform to the journal style.

12. The Journal's Production Editor has the following comments on the figures in your manuscript:

    "Figure 3: Is this available in color? "

    RESPONSE: Yes. We uploaded a version with colors.

    When you submit your revision, art saved in a digital format should accompany it. If your figure was created in Microsoft Word, Microsoft Excel, or Microsoft PowerPoint formats, please submit your original source file. Image files should not be copied and pasted into Microsoft Word or Microsoft PowerPoint.

When you submit your revision, art saved in a digital format should accompany it. Please upload each figure as a separate file to Editorial Manager (do not embed the figure in your manuscript file). If the figures were created using a statistical program (eg, STATA, SPSS, SAS), please submit PDF or EPS files generated directly from the statistical program.

Figures should be saved as high-resolution TIFF files. The minimum requirements for resolution are 300 dpi for color or black and white photographs, and 600 dpi for images containing a photograph with text labeling or thin lines.

Figures should be no smaller than the journal column size of 3 1/4 inches. Art that is low resolution, digitized, adapted from slides, or downloaded from the Internet may not reproduce. Refer to the journal printer's web site (http://cjs.cadmus.com/da/index.asp) for more direction on digital art preparation.

RESPONSE: Figures were created in R and each is being uploaded as a separate pdf file.

SUPPLEMENTAL DIGITAL CONTENT - Include if the author has a SDC file, or if the Editor has suggested SDC.

To ensure a quality experience for those viewing supplemental digital content, the journal's publisher suggests that authors submit supplemental digital files no larger than 10 MB each. The exceptions to this rule are audio or video files, which are acceptable up to 100 MB. When submitting text files or tables as supplemental digital content with your revisions, please do not submit PDFs.

RESPONSE: We adhered to this guideline

***

If you choose to revise your manuscript, please submit your revision via Editorial Manager for Obstetrics & Gynecology at http://ong.editorialmanager.com. It is essential that your cover letter list point-by-point the changes made in response to each criticism. Also, please save and submit your manuscript in a word processing format such as Microsoft Word.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors, that each author has given approval to the final form of the revision, and that the agreement form signed by each author and submitted with the initial version remains valid.

RESPONSE: Indeed, all authors had the opportunity to provide input. All agreements, except Dr. Sit, submitted by the authors remain valid. We uploaded a new agreement signed by Dr. Sit.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Jan 01, 2019, we will assume you wish to withdraw the manuscript from further consideration.

RESPONSE: We thank the editors for extending the deadline to Jan 15, as requested, given the authors' holiday travels.

References cited

1 Tomfohr-Madsen, L. M., Clayborne, Z. M., Rouleau, C. R. & Campbell, T. S. Sleeping for Two: An Open-Pilot Study of Cognitive Behavioral Therapy for Insomnia in Pregnancy. *Behavioral sleep medicine* **15**, 377-393, doi:10.1080/15402002.2016.1141769 (2017).
2 Lee, K. A., Gay, C. L. & Alsten, C. R. Sleep Enhancement Training for Pregnant Women. *Obstetrics and gynecology* **128**, 964-971, doi:10.1097/aog.0000000000001654 (2016).
3 Perach, R. *et al.* The psychological wellbeing outcomes of non-pharmacological inteventions for older persons with insomnia symptoms: A systematic review and meta-analysis. *Sleep Medicianr Reviews* **43**, In Press (2019).
4 Manber, R. *et al.* Efficacy of Cognitive-Behavioral Therapy for Insomnia Combined With Antidepressant Pharmacotherapy in Patients With Comorbid Depression and Insomnia: A Randomized Controlled Trial. *The Journal of clinical psychiatry* **77**, e1316-e1323, doi:10.4088/JCP.15m10244 (2016).
5 Sivertsen, B., Hysing, M., Dorheim, S. K. & Eberhard-Gran, M. Trajectories of maternal sleep problems before and after childbirth: a longitudinal population-based study. *BMC pregnancy and childbirth* **15**, 129, doi:10.1186/s12884-015-0577-1 (2015).

Daniel Mosier

From: Rachel Manber [redacted]
Sent: Wednesday, January 30, 2019 5:39 PM
To: Daniel Mosier
Subject: RE: Manuscript Revisions: ONG-18-2049
Attachments: 4_Appendix 1_(formerly Table 3).docx; 18-2049R1 ms (1-28-19v5) RM.docx

Thank you for your patience.

Please see my response s below

Attached is a revised manuscript as well as a single appendix to replace the two that were previously uploaded, as they were redundant (see response to point #5 below

Rachel

From: Daniel Mosier [mailto:dmosier@greenjournal.org]
Sent: Monday, January 28, 2019 12:15 PM
To: Rachel Manber [redacted]
Subject: RE: Manuscript Revisions: ONG-18-2049

Dr. Manber,

Thank you for sending us your edits in a timely manner. The editors have reviewed your revisions and have a few follow-up questions for you and your co-authors:

1. LINE 245: Difference in remission is ~ 12% which translated to a NNT of ~8. How did you arrive at 3?
2. TABLE 2: Same NNT question
3. LINE 437: Same NNT issue
   For items 1-3 below

   The NNT in this paper is based on predicted values from the survival analysis, not the raw remission rates. The NNT was computed using the formula in the paper below, which calculates NNT at specific time points, taking into account the fact that NNT changes as treatment progresses and that the final remitting event occurred at different times for the two groups.

   Given the more intuitive definition of NNT using the 12% different in remission between the groups, we also included it at all three spots in the manuscript.

   Please note that we also revised Figure 3 legend from “Survival curves derived from Cox Proportional Hazard model” to “Kaplan-Meier survival curves”. This figure is plotting raw data, not predicted values.

   Sjölander, A. (2018). Estimation of causal effect measures with the R-package stdReg. European Journal of Epidemiology. https://doi.org/10.1007/s10654-018-0375-y

   I have not inserted this reference but I can, if you think it will help.

4. FIGURE 2: Please add a citation to this figure within the text of your manuscript.

This was added as a correction in line 235. Thank you for helping me catch the error in referencing this figure.

5. APPENDICIES: To be consistent with Journal style, please rename the citations to “Appendix, Tables 3 and 4” as “Appendix 1” and “Appendix 2,” respectively.

   In doing so I realized that the two appendices are the same only formatted differently. I changed the reference in the text to Appendix 1 and deleted reference to the second appendix. Please also note that I shifted the reference to the appendix form the end of the paragraph to the middle of the paragraph, where I think it fits better

Please let me know if you have any questions or concerns.

Sincerely,
-Daniel Mosier

Daniel Mosier
Editorial Assistant
Obstetrics & Gynecology
Tel: 202-314-2342

From: Rachel Manber [redacted]
Sent: Saturday, January 26, 2019 10:58 AM
To: Daniel Mosier <dmosier@greenjournal.org>
Subject: RE: Manuscript Revisions: ONG-18-2049

Dear Daniel

Please see responses below and also in my responses to the comments in the attached manuscript.

Note two additional documents are attached. One is a revised Appendix, now labeled as Table 4 and a new appendix, Table 3, which per commend below was deleted from the manuscript and made into a second appendix.

Rachel

From: Daniel Mosier <dmosier@greenjournal.org>
Sent: Thursday, January 24, 2019 9:47 AM
To: Rachel Manber [redacted]
Subject: Manuscript Revisions: ONG-18-2049

Dear Dr. Manber,

Thank you for submitting your revised manuscript. It has been reviewed by the editor, and there are a few issues that must be addressed before we can consider your manuscript further:

1. Please note the minor edits and deletions throughout. Please let us know if you disagree with any of these changes.

   I have carefully reviewed the whole manuscript and commented when I did not agree with the edits

2. LINE 11: Elizabeth Rangel will need to complete our electronic Copyright Transfer Agreement, which was sent to them through Editorial Manager.

   Elizabeth tells me she never received a link to complete the copyright agreement. Can you please send (resend) it to her

3. LINE 24: is "for insomnia" redundant?

   The word insomnia is part of the name of the intervention. General cognitive behavioral therapy des not adequately address insomnia. I added the word disorder (see below) to address the apparent redundancy

   Cognitive behavioral therapy for insomnia is an effective treatment for prenatal insomnia disorder.

4. LINE 28: Please re-format to be consistent with our template abstract for RCTs

   Done

5. LINE 31: re our template abstract: Power and sample size comes near the end. How were participants randomly allocated?. Was analysis by intent to treat?

   Moved power to end of method in abstract

   Added description of randomization (blocked)

   Added information about analyzable sample

6. LINE 42: Measured when?

   Added information about timing of measures (weekly)

7. LINE 47: Please provide data from figure 1 as to how many (and 5) who completed assigned therapy

   This information was added

8. LINE 49:
   a. Please be sure this is stated in the body of your paper, tables, or figures. Statements and data that appear in the Abstract must also appear in the body text for consistency.

      Done

   b. Please provide data from first row of Table 2 here please.

      Done

9. LINE 53: This p-value was added to line 271.

   Thank you

10. Line 70: “CBTI” and “CTRL” have been expanded throughout the paper (except tables and figures) because the abbreviations are not used by the journal. Please review the edits, since you may not need to include “for insomnia” in every instance.

    Whereas I retained “for insomnia” in reference to cognitive behavioral therapy, I deleted it in most instances where I was referencing the control

11. LINE 87: If what I deleted here is not included it later, please add it back but not here

    I moved some of the information. See response to comment in the body of the revised manuscript

12. LINE 106: Is a steroid inhaler really a stimulant?

    I deleted the example, as it is not needed

13. LINE 204: Detect when?

    Added. Note that mixed effect models examine all available weekly data from baseline to post treatment

14. LINE 207: Please review the responses added to each question and edit as needed.

    Done

15. LINE 210: Please give dates here

    Added

16. LINE 216: Please everywhere replace "arm" with "group" when talking about the randomization groups

    Done

17. LINE 232: Added from abstract.

    Addition is OK

18. LINE 252: Please here reiterate findings for primary outcome.

    Done

19. LINE 292: Please provide this percentage

    Added

20. TABLE 3: Please move to Appendix

    I deleted and attached as an appendix, replacing “Arm” with “Group”.

    We already had another appendix which is now labeled as Table 4 and where I replaced “Arm” with “Group”. I attached this one as well.

I changed references to the old appendix to read: Appendix, Table 4

Please let me know if you have any questions. Your prompt response to these queries will be appreciated; please respond no later than COB on **Monday, January 28th.**

Sincerely,

-Daniel Mosier

Daniel Mosier
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Web: http://www.greenjournal.org

From: [redacted]
To: Stephanie Casway
Cc: Daniel Mosier
Subject: RE: O&G Figure Revision: 18-2049
Date: Friday, February 1, 2019 1:47:02 PM

Stephanie

I like the red box in Figure 1
Figure 3 looks OK

For the legend of Figure 2: Since the figure key labels one of the curves as CTRL, I think the word CTRL needs to be explained in the caption
It should read

> Figure 2. Modell estimated changes in insomnia symptom severity for the intervention (cognitive behavioral therapy for insomnia, CBTI) and control therapy for insomnia groups (CTRL).

The same applies to the cation of Figure 3. More important is that the edits you made changed the meaning so it is now incorrect

> Figure 3. Survival curves derived from Kaplan-Meier analysis. Time to insomnia nonremission for the intervention (cognitive behavioral therapy for insomnia, CBTI) and control conditions (CTRL). The analysis was based on all participants who provided at least one post-baseline Insomnia Severity Index score; Remission is defined by Insomnia Severity Index less than 8. Hazard ratio=2.55 (95% CI: 1.51 to 4.32). Number needed to treat for the difference between rates of remissions equals 8. Number needed to treat effect size for the model, considering the fact that the final remitting event occurred at different times for the two groups, equals 3.05 (95% CI: 1.53, 4.57).

Rachel

From: Stephanie Casway <SCasway@greenjournal.org>
Sent: Friday, February 1, 2019 10:32 AM
To: Rachel Manber [redacted]
Cc: Daniel Mosier <dmosier@greenjournal.org>
Subject: RE: O&G Figure Revision: 18-2049

Good Afternoon Rachel,

Thank you so much for your review and edits. Daniel mentioned that you had been very responsive to his emails, so I was concerned that my messages got trapped in a spam folder.

Attached you will find updated versions of Figure 1, Figure 3, and the legend. I framed the "included in the analysis" boxes in red and defined it in the legend to be consistent with journal style. I also made a few edits to the legends per journal style.

Please let Daniel and I know if these edits are okay, or if any more are needed.

Have a great day!

From: Rachel Manber [redacted]
Sent: Friday, February 1, 2019 12:43 PM
To: Stephanie Casway <SCasway@greenjournal.org>
Cc: Daniel Mosier <dmosier@greenjournal.org>
Subject: RE: O&G Figure Revision: 18-2049

Stephanie

I have no idea why your emails escaped my attention. I am glad you reached out to Deirdre as her email alerted me to yours

I carefully reviewed all three figures

Figure 1 is accurate and I like the revised display. I think it will be ideal with the boxes labeled "Included in analysis" are highlighted (using shading). This will make it clear the we included women who did not start or complete treatment.

Figure 2: OK as is

Figure 3: Your revision is OK but I am realizing that the y-axis is between 0 and 1 representing proportion rather than percent. The easiest way to modify is to label the axis as "proportion of nonremission" or "Nonremission (proportion)"

Regarding figure captions:

Figure 1 captain is OK

Figure 2 caption: slightly revised as ffollows

> Figure 2. Modell estimated changes in insomnia symptom severity for the intervention and control groups. CBT=cognitive behavioral therapy for insomnia; CTRL=control therapy for insomnia**.**

Figure 3 caption: This was modified following query by Daniel Mosier (cc-ed). I tried to merge your edits with the revision I sent him a couple of days ago

> Figure 3. Survival curves derived from Kaplan-Meier analysis. Time to insomnia nonremission

for the intervention (CBTI) and control (CTRL) conditions. The analysis was based on all participants who provided at least one post-baseline ISI score. Numbers at risk (i.e., nonremission) are displayed under the x-axis. Remission is defined by Insomnia Severity Index (ISI) < 8. The Hazard ratio=2.55 [95% CI: 1.51 to 4.32]. NNT for the difference between rates of remissions=8. NNT effect size for the model, taking into account the fact that the final remitting event occurred at different times for the two groups=3.05 [95% CI: 1.53, 4.57]**.**

Sorry for the delayed response

Rachel

From: Stephanie Casway <SCasway@greenjournal.org>
Sent: Wednesday, January 23, 2019 11:19 AM
To: Rachel Manber [redacted]
Subject: O&G Figure Revision: 18-2049

Good Afternoon Dr. Manber,

Your figures and legend have been edited, and PDFs of the figures and legend are attached for your review. Please review the figures CAREFULLY for any mistakes. In addition, please see our query below.

AQ1: Note that we have added an exclusion box to Figure 1. If this is incorrect, please let me know.

PLEASE NOTE: Any changes to the figures must be made now. Changes at later stages are expensive and time-consuming and may result in the delay of your article's publication.

To avoid a delay, I would be grateful to receive a reply no later than Friday, 1/25. Thank you for your help.

Best wishes,

Stephanie Casway, MA
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