Author’s response to reviews

Title: The Effect of Cognitive Behavioral Therapy for Insomnia in People with Type 2 Diabetes Mellitus, Pilot RCT Part II: Diabetes Health Outcomes

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Author’s response to reviews:

Point-by-Point response to reviewers’ comments

Dear Editorial Office of BMC Endocrine Disorders and the reviewers,

The authors on the paper titled “The Effect of Cognitive Behavioral Therapy for Insomnia in People with Type 2 Diabetes Mellitus, Pilot RCT Part II: Diabetes Health Outcomes” appreciate the work and effort that have been done since the submission. We accept the opportunity to further this submission by addressing the reviewers’ comments. In this document, you will find the reviewers’ comments addressed point by point. To aid in the clarity of where revisions were made, we submitted a version of the revised manuscript with the revisions highlighted in yellow.

Reviewer 1 point #1

Comment: In figure 1, n=13 in Pre-post change analysis for both CBT-I and HE group. But in table 2, baseline values are given for n=14 in both the groups. Shouldn't the baseline values be for 13 participants? Could you clarify on this?
Response: Thank you for your question. We did the mean change analysis for who only completed the study. However, we still presented the descriptive values (mean and standard deviation) for all participants at the baseline. To clarify that, we added more information about the descriptive values and the main analysis on lines 231-235.

Reviewer 2 point #1

Comment: Language edition is needed.

Response: After addressing the reviewers’ comments, we have hired an English editor to proofread the manuscript. Thank you for bringing this point to our attention.

Reviewer 2 point #2

Comment: "Insomnia symptoms" - is this expression used throughout the manuscript the most appropriate?

Response: Thank you for your question. We used a screener (insomnia Severity Index) that indicated the severity of insomnia symptoms including difficulties falling asleep, maintaining asleep and/or waking up too early, which impact the daytime functioning. Thus, using the term insomnia symptoms throughout the paper is appropriate. Studies that used diagnostic criteria of insomnia may refer to chronic insomnia in their work.

Reviewer 2 point #3

Comment: Since this is an endocrine journal, please briefly summarize what CBT consists on (compared to other psychotherapy modalities).

Response: Thank you for this suggestion. We have added more information about the components of CBT-I in the introduction and the method sections (lines 96-99 and lines 181-220).

Reviewer 2 point #4

Comment: Improvement of the circadian cycle misalignment, that has intimate correlations with glucose metabolism

Response: We highly agree with the reviewer. We found the provided statement should be pointed out in the introduction to strength the rationale of our study on lines 103-105.

Reviewer 2 point #5

Comment: "the effects of…", better than "the effect of…"

Response: Thank you for your suggestion. We agree with the reviewer’s comment. This was addressed throughout the manuscript.
Reviewer 2 point #6

Comment: Authors should make clear why they divided their results into two parts. It does not seem too much data to fit within a sole work.

Response: This project resulted in 2 manuscripts. The sleep outcomes (Part I) were reported separately in which its paper recently received conditional acceptance from the Behavioral Sleep Medicine (BSM) Journal. Initially, we submitted both manuscript in the BSM journal. However, the editor suggested to consider the second part of this intervention to be submitted to a journal with scope in diabetes clinical interests and we agreed with the editor’s decision. To address the reviewer’s comment, we added more information about the aim of both trials in the introduction section on lines 111-117.

Reviewer 2 point #7

Comment: How can we assume that the full improvement of glycemic control in response to CBT is due to improvement of insomnia, and not secondary to other psychological domains?

Response: This is a great question. Although CBT-I is designed to address insomnia symptoms, other factors (such as psychological symptoms) could be improved following CBT-I. Thus, we were not able to determine if the improvement of glycemic control was fully mediated by insomnia severity or psychological symptoms. The reviewer’s question made us to add this point as limitation to be considered in future work on lines 345-348.

Reviewer 2 point #8 (Introduction)

Comment: Please specify the differences between Parts I and II of the clinical trial. Apparently, part II does not add any new information. Make it clear b 1st paragraph - 1st and 2nd sentences are repeated, and the 2nd sentence is a little bit confusing.

Response: we have specified the difference between Part I and Part II on lines 111-113 and 321-323. Also, the second sentence on the paragraph 2 was modified to improve clarity on the line 73.

Reviewer 2 point #9 (Introduction)

Comment: 2nd paragraph - "other studies have shown insomnia symptoms to be a mortality risk, even after controlling for comorbidities" - do authors mean: "other studies have shown that insomnia may independently increase mortality rates", or "other studies have shown that insomnia may be at increased risk of earlier death, irrespectively of comorbidities"?

Response: We see the reviewer’s comment. We agree that our previous sentence made confusion for the reader. The sentence was modified based on the reviewer suggestion and the referenced studies on lines 82-83.

Reviewer 2 point #10 (Introduction)
Comment: 3rd paragraph - "The American Academy of Sleep Medicine recommends treating insomnia symptoms using Cognitive Behavioral Therapy for Insomnia (CBT-I)." - This sentence should be rethought. Suggestion: "Among therapeutic options for insomnia, the American Academy of Sleep Medicine recommends the employment of Cognitive Behavioral Therapy for Insomnia (CBT-I) as first-line therapy, since CBT can be superior when compared to sleep medications".

Response: We highly appreciate your suggestion. Your valid suggestion was utilized in the manuscript on lines 88-91.

Reviewer 2 point #12 (Results)

Comment: Authors should provide the effects of CBT on insomnia, and then correlate them with improvements of glucose metabolism. Direct correlations between CBT and glycemic control do not allow us determine whether these improvements were mediated by improvement of sleep quality or not.

Response: The reviewer brought up an interesting research question that could be addressed in future studies. Due to the nature of pilot studies, we did not account for different analysis in our initial power calculations. In addition, we were not interested initially in the mediation analysis during protocol establishment. We want to approve first the effects of the intervention on different sleep parameters and health outcomes. To satisfy the review’s comment, we added this interesting research question in our discussion to facilitate future study answering this question in depth on the lines 345-349.

Reviewer 2 point #13 (Discussion)

Comment: Authors should explore in a deeper manner the molecular, metabolic, and hormonal underlying mechanisms that may explain the link CBT-insomnia-improvement of glucose. Some of the sentences are repeated from the introduction and results. Please state what does Part II add in terms of novelties, in relation to previous studies and to Part I.

Response: This is valid point and we appreciate allowing us to explain more in depth the underlying mechanisms. We have already explained possible physiological mechanisms that might be interested to the readers. In addition, we add other underlying mechanisms that explain the possible metabolic and hormonal changes following sleep improvements on lines 309-325.

Reviewer 3 point #1

Comment: Details about antidiabetic treatments should be in the text in order to better characterize the population.

Response: We see the reviewer’s comment might be interested in pharmacologists. We did not specify the combined effect of sleep and diabetes intervention, and the exact dosage of medications were not collected. We found this should be added in the limitation of this study on lines 340-342. As this point could be addressed in future studies.
Reviewer 3 point #2

Comment: Cognitive Behavioral Therapy for Insomnia (which therapeutic techniques, Alexander technique etc.) should be detailed for the reproducibility of the treatment. Cognitive Behavioral Therapy for Insomnia.

Response: Thank you for this valid point. We have updated the intervention section to explain the provided intervention. Also, we have added and referenced the used protocol for readers (lines 171-226).