Author's response to reviews

Title: Sleep to lower elevated blood pressure: study protocol for a randomized controlled trial

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Author's response to reviews: see over
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Editor,
Trials

Dear Editor,

Thank you for considering our manuscript for Trials. The comments from the reviewer were very beneficial and we believe they have resulted in a greatly improved manuscript. We have made every effort to address each of the points raised by the reviewer, itemized below.

Comment 1
An important limitation is the inclusion of patients with undiagnosed OSA. The proposed intervention will not improve OSA and therefore the ability to detect an effect of CBT could be undermined. The authors should address why this is not a concern.

Response 1
We agree with the reviewer that patients with undiagnosed OSA could limit our ability to detect a treatment benefit with CBT. However, due to financial constraints, we were unfortunately unable to conduct polysomnography testing on potential participants. We elected to exclude patients with a known diagnosis of untreated OSA as an alternative best option. We have the following text to the manuscript on page 31, paragraph 3: “A fifth potential limitation is that patients with undiagnosed OSA may be included in this study, which could undermine our ability to detect a true treatment effect, given such patients may not be expected to improve with the intervention. Thus, we have excluded patients with a known diagnosis of treated OSA, to minimize this potential limitation”.

Comment 2
Another important limitation is there is no objective assessment of sleep duration and quality, which is the primary target of the intervention arm. Subjective sleep estimates are only modestly correlated with objective measures.

Response 2
The aim in this study was to determine the efficacy of a behavioral intervention targeting sleep that could potentially be implemented at a population level. Thus, we wanted an intervention that was simple, easy to implement, with minimal disruption to a patient’s lifestyle. We therefore decided to assess sleep duration subjectively, via patient self-reporting. Our primary outcome measure in this study is a reduction in SBP, rather than an objective measure of sleep duration or quality.
Comment 3
The text states, “Participant adherence to the intervention will also be measured, and adjusted for using sensitivity analysis.” but they do not indicate how adherence will be measured. The authors should address why this is not a concern.

Response 3
We collected data on the number of online sleep sessions completed, as well as self-reported sleep efficiency data based on patient sleep diaries. We intend to look at both of these variables as measures of adherence, and will analyze the data for evidence of a dose response, e.g. relationship between reduction in SBP readings and number of online sleep sessions completed. The following text has been added to the manuscript on page 25: “For example, we will analyze the data for evidence of a dose response relationship between degree of reduction in SBP and number of online sleep sessions completed.”

Comment 4
A third concern is that the control group gets one 30-minute session (usual care) but the intervention group gets an internet intervention with multiple sessions. How will investigators know it is the change in sleep duration and quality that had an effect and not just the extra attention associated with the internet interaction? The authors should address why this is not a concern.

Response 4
We agree with the reviewer that differences between the treatment arms could be partly explained by differences in attention between the two treatment groups, which is an important consideration in trials of behavioral interventions. However, given this is a phase II, proof of concept study, with the aim of maximizing the chances of detecting a true treatment effect, we elected not to use an attention placebo in the control arm. If a significant treatment effect is observed in this pilot study, a larger scale phase III trial will be required, with the inclusion of an attention placebo in the control arm. We have added the following text to the manuscript on page 31 paragraph 3: “Finally, our results could be subject to attention bias, due to differences in the level of attention provided to the two treatment groups. However, given this is a phase II, proof of concept study, with the aim of maximising the chances of detecting a true treatment effect, we elected not to use an attention placebo in the control arm. If a significant treatment effect is observed in this pilot study, a larger scale phase III trial will be performed, with the inclusion of an attention placebo in the control arm, in order to demonstrate the effectiveness of this intervention in a broader population of patients for primary and secondary prevention of CVD.”

I would be happy to address any further comments that you may have. Thank you for considering our paper for Trials

Yours sincerely,

Dr. Emer McGrath, MB, PhD, MRCPI, MRCPUK