

## Peer-review Comments and Author Responses

### Reviewer 1 (comments in the Word document)

1. This paragraph should also emphasize the adherence issues commonly found in chronic and commonly asymptomatic disease such as HTN.

Thanks, we agree on emphasizing the challenge, yet not as detailed to avoid the focus of the manuscript. We added the following sentence which is also addressed in the corresponding bibliographic reference: “Considering the challenge of adherence to antihypertensive medication, non-pharmacologic strategies have been of increasing interest among the medical and patient population.”

*2. Would like to see a more concise sentence: “the WHO estimated prevalence of HTN is 1.28 billion*

Thanks for the observation, we modified the sentence according to your suggestion.

*3. This paragraph should also emphasize the adherence issues commonly found in chronic and commonly asymptomatic disease such as HTN.*

Thanks, we agree on emphasizing the challenge, yet not as detailed to avoid the focus of the manuscript. We added the following sentence which is also addressed in the corresponding bibliographic reference: “Considering the challenge of adherence to antihypertensive medication, non-pharmacologic strategies have been of increasing interest among the medical and patient population.”

*4. There should be also mention of this strategy across the different spectrum of prevention CVD strategies. As I would assume is a safe option to use for primary and secondary CVD prevention.*

Thank you. As requested, we added evidence of CVD prevention in the last two sentences of this paragraph.

*5. It would be interesting to mention what type of hypertensive and prehypertensive patients were assessed. As hypertension affect from middle aged adults to the elderly, or primary or secondary prevention. And the BP goal is also individualized. So it would be interesting for the reader to know more about this.*

Thanks for your recommendation. More detailed inclusion and exclusion criteria was included regarding the prehypertensive and hypertensive adult population included.

*6. It is not clear how this reduction was documented. It was a mean home BP? Or Office BP?*

Thank you for the observation. Clarification of the method utilized in the included articles in the said literature review to measure and compare variations in BP pre- and post-interventions.

*7. Depending on this, a following sentence explaining the relevance of this finding in terms or reduction of cardiovascular outcomes would be appropriate. Because we are not interested solely on the reduction of BP, but how this reduction have shown to be reduced cardiovascular outcomes.*

Thank you for the observation. Clarification of the method utilized in the included articles in the said literature review to measure and compare variations in BP pre- and post-interventions. Moreover, as suggested, evidence of the effect of BP lowering in the reduction of CVD and all-cause mortality was added in an additional sentence following the clarification mentioned above.

*8. It would be interesting to add [clinicaltrials.gov](https://clinicaltrials.gov) to have a reference of future upcoming trials using this intervention (or the lack of registered trials for upcoming years).*

*9. I would rewrite this sentence as “The detailed search strategy can be find in the supplementary appendix”*

Thank you for the suggestion. We have replaced the sentence accordingly.

*10. Although it is understandable to use this as a criteria, would be interesting to mention specifically why or if this limitation was addressed by the authors during the reviewing process.*

Thanks for your advice. The decision of only open access studies was to avoid possible conflict regarding the use of Sci-Hub which may rise several concerns which we decided to avoid. We consider it is implicitly understood and may not need to be addressed.

*11. Is there a specific reason to exclude patients older 65 years of age? I would consider also excluding patients with any type of respiratory illness that significantly alters normal breathing physiology or special populations (ie, pregnancy).*

The decision to exclude patients older than 65 years of age was to avoid the isolated systolic hypertension related to age. No other special population was considered such as pregnancy in order to obtain a broader result that may be generalized to a real-world population focused within the previous mentioned ranges of age. Nevertheless, studies included in the study selection process did not include special populations overall.

*12. Why were these terms excluded and how could these have impacted the articles screened?*

These terms such as ‘yoga’ and ‘Qigong’ were excluded since, although they are also considered as non-pharmacologic treatment strategies, they differ substantially to deep breathing technique, since they both include an enhancement of certain physical activity that is performed. If articles with these terms would have been screened, a more robust sample of manuscripts would have resulted, as well as the scope of the aim of this review would have diluted the focus of breathing technique, which is a less addressed non-pharmacologic treatment strategy in comparison to Yoga and Qigong.

13. *Because the mini review has 3 different objectives, I would argue is hard to comprehensively review these 3 different objectives solely using the abstract or even the methods section without including the results of the article. Because the articles included were 4, the authors could consider also review the results section to confirm all the possible information is included in the review.*

Considering the results section is based in the objectives and methods established in each manuscript, we considered no need to evaluate eligibility in results. Nevertheless, results were briefly summarized in the abstract of each screened manuscript.

14. *The figure 1 is clearly explained, but it lacks details in the screening process. 118 articles were excluded, but it is not specified why they were excluded. For this specific details, I would advise to use the recommended figure 1 found in the official PRISMA website for screening only databases. Similar to my comment above, I would add a second review for the results of the 4 articles included to confirm all the information and details were extracted from the articles.*

Thank you for the suggestion. It was not written in the manuscript, but each article was revised by two reviewers, being the second reviewer common to all four articles. Specification to this process was added, as requested.

15. *This section is hard to follow. And even when reviewing the tables, it is hard to understand without stopping to review each value. I would recommend for the authors to make a small simplified table with the intervention and mean effect. And small annotations that the authors consider essential, so the reader could have a broad idea of the specific effects and compare them*

Thank you, we will add the suggested table.

16. *I would say it is debatable how safe is the intervention based on 1 of the 4 studies, while the others didn't assessed it. I would change it to a less debatable sentence by emphasizing only 1 study assessed the side effects. I think is appropriate to add the % in addition to the number of patients. And if there is also any relevant information about them (did they have history of any type of arrhythmia? Or psychological/psychiatric comorbidity for example?)*

Thank you for the suggestion. As requested, we have added the percentages of the patients who presented the described adverse effects. Unfortunately, there is no additional demographic or clinical information on these patients.

17. *The authors should also emphasize more about some important differences in the methodology of the articles included:*

- *The different types of BP assessed in the different trials (24 hour, BP diary, home-based measurements, office-based measurements)*
- *The population assessed in the studies (comorbidities, overall age, etc)*
- *Addressing the limitations of not exploring more databases*
- *Reason for exclusion of most of the articles screened*

- *Limitations for assessing safety of the intervention as well as the difference of device-based or not*
- *Number of patients included in these trials, as well as regions assessed (Asia 3 studies)*

Thank you very much, while these are incredibly helpful suggestions, limitations in word count constrained us from discussing more specific details about the studies reviewed. However, these are suggestions that could be addressed in supplemental or indexed pages of this paper.

*17. I agree with the conclusion of the authors. Although the authors explore the safety and adherence, I would organize describing the efficacy as the primary objective and the others as secondary, because the title of the article as well as the conclusion only focuses on the efficacy of the intervention and doesn't mention the other 2 goals. In addition, because the other 2 were not fully assessed because of the reduced number of articles, it would be biased to describe further conclusions about adherence of safety.*

Thank you very much! While the objectives of this mini-review were listed as following: “(1) assess the overall BP-lowering efficacy of breathing techniques in HTN, (2) compare the efficacy of device-guided versus non-device-guided DBT, and (3) assess the safety and adherence rate of DBT;” we believe, each objective was observed considering the literature under review. Yet, we agree that these objectives can be revised to highlight efficacy as the primary objective and safety and adherence as secondary objectives. Consequently, the conclusion should address the realization of these objectives in relationship to the limitation due to the lack of studies that properly assess the safety and adherence of DBT.

*18. It would be preferable if there are more recent references that explore the role of ANS. Specially considering the nature of the mini-review*

Indeed, thank you for bringing this to our attention. Although this article by Amerena and Julius, marks a clear ‘before and after’ our understanding of the relationship between the ANS and hypertension; more recent references can be of used to highlight the association between the elevations in BP and the risk of CVD. For example, this reference can be replaced by the following reference that just recently analyzed this same relationship and made the corresponding conclusion.

## **Reviewer 2**

- 1. I recommend you use fewer abbreviations in the abstract. Your abstract should be more precise.*
- 2. I recommend using Medline instead of Pubmed. Pubmed is the search engine, not the database.*
- 3. In your title, you included Elevated Blood Pressure as the condition treated by the deep breathing technique, but you didn't include it in the literature search. Please, explain.*
- 4. I recommend reviewing the keyword. Some are not listed in the MeSH terms.*

## **Reviewer 3**

*5. The results obtained should be discussed in relation to the research question and the objectives, as well as the consistency (similarities or discrepancies with the results of other studies). It is advisable to highlight it.*

*6. It is a very interesting review, however, you need to look for inconsistencies, for example, the number of papers retrieved from the literature. You are showing different numbers in the abstract, methods and figure.*

### **Author response to reviewers 2 and 3**

Among some of the changes made through the document, I may summarize the following: Changes in coauthors order was made according to the active participation during the following process. Grammatical and spelling corrections were made. Along the introduction section, we briefly emphasized the challenge of treatment adherence in hypertension, evidence on cardiovascular disease prevention related to deep breathing techniques, and we also modified the Figure 1 flowchart accordingly to the revised bibliography considered. In results section we modified and corrected Table 1 with reviewers' suggestions. Further recommendations along Discussion and Conclusion sections were discussed along the "comment notes" within the word document.