REPLY

Response to commentary by Heidari and Arabzadeh on "Worldwide and regional prevalence rates of co-occurrence of insomnia and insomnia symptoms with obstructive sleep apnea: A systematic review and meta-analysis"

We recently reported the prevalence rates of co-occurrence of insomnia and insomnia symptoms with obstructive sleep apnea (OSA) in an extensive meta-analysis [1]. Drs. Heidari and Arabzadeh commented on our work and raised several methodological issues that need to be considered in conducting meta-analytic studies [2]. We greatly appreciate their efforts and interest and, for the most part agree, with their comments regarding the necessity of taking proper care in conducting this type of study. However, as indicated below, many of the concerns they raised were fully addressed in our paper.

First, they expressed concern that our work may not comply with the standard guidelines for conducting a meta-analysis such as the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [3] and MOOSE [4] statements, because 1) our study was not registered, and 2) our study did not mention whether we followed a specific meta-analysis guideline. It should be noted that whether a meta-analysis must be registered before the work begins is somewhat controversial. Takkouche and Norman [5] stated that "*Meta-analyses are published only after having passed through two filters: peer review, and an editorial decision, which suffice to decide whether a meta-analysis is good enough and novel enough to deserve publication. An additional committee or register does not increase the quality of what is published: it only weakens the decision capacity of editors and reviewers, and increases bureaucracy.*" Although the editor of a scientific journal traditionally encourages authors to register their meta-analysis protocol, it is not mandatory in most scientific journals, including Sleep Medicine Reviews. Indeed, with the exception of registering a protocol, our meta-analysis complied with the PRISMA statement regarding how to perform a high quality meta-analysis [3]. As clearly reflected in our Methods section and in Tables S1–S8 of our detailed 45 page supplementary file (see original manuscript [1]), we provided extensive details of how our meta-analysis was performed, including our search strategies for all databases, information regarding contacting original authors of the included studies, the selection process of included studies, and which included study was used in each analysis, etc. Comparing this information to that in the PRISMA checklist easily demonstrates that our meta-analysis complied with the PRISMA statement [3]. We did not state that our systematic review and meta-analysis followed the PRISMA statement in our manuscript because we did not register our study.

Second, Heidari and Arabzadeh expressed concern that "*there was no final conclusion of Egger's tests and its P value in the meta-analysis.*" However, we clearly reported our findings from Egger's tests (no publication bias was found) in the Results section of our study and we reported their P values in Figure S6 of our supplementary file (see original manuscript [1]). We also commented on our findings with Egger's test in the Limitations section of our Discussion. Furthermore, Heidari and Arabzadeh suggested that Egger's test may have been inappropriately used in our meta-analysis, and stated that "*for the dichotomous data, the outcome of the measurement is based on OR [odds ratio], and the Harbord test and Peters test should be preferred.*" We do not believe that this point is relevant for our study because exploring the pooled prevalence in a single group and exploring the difference of prevalence data between groups are two different cases which impacts choice of method for assessing publication bias. To our understanding, when performing a meta-analysis exploring differences in prevalence data between two groups, the outcomes are measured based on ORs. In this case, Peter's test (for group comparisons) is preferred to assess publication bias [6,7]. However, we only explored the pooled prevalence rates of insomnia symptoms in OSA patients without comparison to those in a control group. When only exploring the pooled prevalence data in a single group without controls, Egger's test is still a widely used and rigorous method to assess publication bias in meta-analytic studies (e.g., [7–9]).

Third, Heidari and Arabzadeh were also concerned with the high heterogeneity of our meta-analysis findings. For a prevalence meta-analysis, the data can be sourced from studies with any study design and with different demographic characteristics of participants, different diagnosis criteria for diseases, different geographical locations, etc. These factors, indeed, contribute to high heterogeneity, but our study is not a special case for this issue. Indeed, high heterogeneity is a virtually universal concern and is very commonly seen in meta-analytic studies of prevalence data [9–11]. However, subgroup and meta-regression analyses approaches allow the exploration of possible sources and positing potential explanations for the high heterogeneity. By performing subgroup and meta-regression analyses, we comprehensively explored the potential sources of heterogeneity where possible (e.g., the potential effects of sex, age, and body mass index of the participants, recruitment setting, diagnosis criteria of OSA/insomnia, oxygen desaturation for hypopnea, clinical intervention, etc.) on our pooled effect sizes. The outcomes are clearly shown in our Results section and in our supplementary file (Table S12–S20, see original manuscript [1]), and we also discussed these findings

in our study. Therefore, we do not understand the conclusion of Heidari and Arabzadeh that "*In this paper, the heterogeneity of groups is high, but the source of heterogeneity has not been explored.*"

In summary, we agree with Heidari and Arabzadeh "*that meta-analysis is an important means of evidence-based medicine*" and that using established and validated protocols and procedures is imperative for providing confidence in the results and in comparisons across studies. We did exactly that in our meta-analytic study of insomnia and OSA.

Acknowledgements

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27 March 2019
Available online 19 April 2019