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Reply to Liu et al.: "Effects of Cognitive Behavioral Therapy for Insomnia (CBT-I) on Quality of Life: A Systematic Review and Meta-Analysis"

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The letter by Liu et al. (1) questioned our use of choosing the standardized mean difference (SMD) to assess effect sizes in our paper "Effects of cognitive behavioral therapy for insomnia (CBT-I) on quality of life: A systematic review and meta-Analysis" (2). Choosing the proper effect size to include in a meta-analysis is always an important choice for the researcher (3). This choice is always influenced by how the findings are reported in the primary studies and to what extent the level of homogeneity of the scales used for assessing the desired outcome (4). For dichotomous variables, the relative risk family effect sizes including the relative risk (RR), the odds ratio (OR), and the risk difference (RD) are commonly used effect sizes. For continuous variables, either the mean difference (MD) or the SMD are preferred effect sizes (5).

Although MD is a good choice to calculate and report clinical significance of an intervention, its selection as effect size for meta-analysis depends on having reported minimum clinically important difference (MCID) values for each scale and the similarity of the measurement scales used for assessing the outcome variable through selected studies. According to the Cochrane Handbook for Systematic Reviews of Interventions (5), the *"selection of summary statistics for continuous data is principally determined by whether studies all report the outcome using the same scale when the MD can be used"* (Section 9.2.3). In this regard, SMD is one of the most appropriate choices for mean difference in the conditions of selection of the outcome with a continuous quantitative scale and the presence of heterogeneity in the selected studies for meta-analysis (6).

Considering these issues and due to the fact that the selected studies in our meta-analysis (2) reported the outcome (i.e., changes in the quality of life) in a continuous quantitative manner, the composition based on RD was not possible. Also, variation in scales used to assess the quality of life (QoL), meant that SMD was the best choice for estimating pooled effect size. In this case, any modeling for calculating RD was possible only based on the results of the SMD as the only finding that were reported in the selected papers. In our opinion, this modeling based on SMD values, would be a repetition and not increase the level of information for the reader. For this reason, the selected effect size for the aforementioned review (2) was the SMD, given that its data were extractable based on the results reported in the studies. However, assessing MCID and RD based on clinical significance is also an important suggestion for future studies.

Liu et al. (1) also suggest we should have used GRADE (Grading of Recommendations Assessment, Development and Evaluation) to assess overall study quality. It is worth mentioning

that we carefully checked the methodological quality of the selected studies using Cochrane ROB Assessment Tool (7). The results of the quality assessment are shown in Figure 1 of our review (with details) and the tables representing the characteristics of the selected studies based on the design and specific characteristics of the intervention were presented separately in our review (2). Therefore, we include the table of evaluation of the quality of evidence based on GRADE criteria for the studies we reviewed (see Table 1). The GRADE table – which is consistent with main published paper (2) – shows that the quality level of the studies is low and there is a need for conducting higher methodological quality studies, especially blinded studies. However, it is worth mentioning that this point was originally noted in the discussion of the findings in our review (2): *"Moreover, most studies synthesized in the present systematic review and meta-analysis did not utilize blinding to control placebo effects. Therefore, it is possible that the findings of CBT-I are likely to be overestimated"* (p. 15).

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Table 1. GRADE profile of effects of cognitive behavioral therapy for insomnia (CBT-I) on quality of life									
	Quality assessment							Summary of finding	
	Participants	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall quality of evidence	Pooled estimates	Moderators
Overall outcome	24 studies (19 RCT, 5 trials) comprising 1977 participants (808 in intervention group)	Moderate risk of bias (10 blinded and 9 not blinded) -1 score	High heterogeneity (I^2=84.5%) -2 score	No serious indirectness	Probable imprecision -1 score	No publication bias	7-4=3 Low ⨁◯◯◯	SMD: 0.47 (95% CI: 0.22-0.72)	Type of blinding, number of sessions, and participants' mean age
Face-to-face CBT-I on QoL in RCT studies	11 studies comprising 729 participants (375 in intervention group)	Moderate risk of bias (8 blinded, 3 not blinded) -1	High heterogeneity (I^2=87.5%) -2 score	No serious indirectness	Serious imprecision -2 score	No publication bias	8-5=3 Low ⨁◯◯◯	SMD: 0.46 (95% CI: 0.01-0.90	Type of blinding and number of sessions
Online CBT-I on QoL in RCT studies	8 studies comprising 820 participants (419 in intervention group)	High risk of bias (two blinded,	High heterogeneity (I^2=88.3%) -2 score	No serious indirectness	Serious imprecision -2 score	No publication bias	8-5=3 Low ⨁◯◯◯	SMD: 0.47 (95% CI: 0.02-0.92	Type of blinding and participants' mean age

		other not blinded) -1 score							
CBT-I on QoL in one group pre- and post-treatment trial	5 studies compromising 178 individuals	High risk of bias (all not blinded) -2 score	Moderate heterogeneity (I^2=52.9%) -1 score	No serious indirectness	Probable imprecision -1 score	No publication bias	6 -4=2 very low 	SMD: 0.46 (95% CI: 0.12-0.80)	No moderator was detected