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LETTER TO THE EDITOR

Methodological issues in meta-analysis of the metformin effects on simple obesity

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Letter to the Editor

Dear Editor,

I have read with grand interest the recent meta-analysis by Dr Ning and colleagues [1], published in volume 62, issue 3, December 2018 of *Endocrine*. The authors found that among overweight or obese subjects, the metformin was effective in reducing body weight, as well as it did not induce hypoglycemia as a side effect. However, while this article is well written, there were some methodological issues in using the fixed-effect model that I would like to address.

This study used a fixed-effect model (Figure 5) for summarizing the mean difference based on the I^2 heterogeneity statistic. However, this approach of model choice is questionable [2]. First, the fixed-effect model is justified plausible if assuming that all the studies included in the analysis are functionally identical, such as the same population or treatment process given, and that the goal is to compute the common effect size for only an included population, but these assumptions are barely met in practice. Conversely, the random-effect model aims to estimate the mean of a distribution of effects, and more importantly, it allows to generalize the conclusions beyond the observed studies to other studies with similar characteristics. Second, the model choice simply based on the statistical tests is not suggested, since these tests have lower power to detect heterogeneity, especially when the number of included studies is small [2]. Third, a further discrepancy between the two approaches is that the standard error is smaller in the fixed-effect model than the random-effect model, and this leads to a conservative confidence interval (CI) for the fixed-effect model. For instance, when using a random-effect model with Hartung and Knapp adjustment [3] for figure 5a of Ning et al.'s study, not only the CI became wider, but the summarized mean difference (MD) was no longer borderline-significant, and even altered the signs (summary MD = 0.03, 95% CI: –0.11–0.16; Fig. 1). Therefore, the appropriate use of either a fixed- or a random-effect model ought to be made on the basis of prior knowledge about the constituent studies, rather than the single-point estimates.

In conclusion, I truly believe that the work by Dr Ning et al. will provide valuable insight into further research on use of metformin, and I hope that these methodological issues could be considered and discussed.

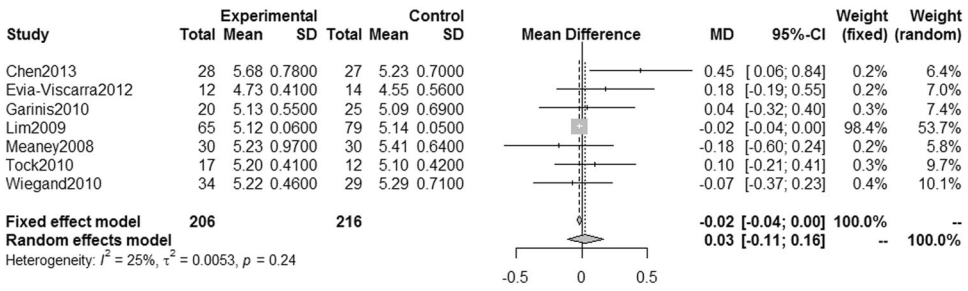

Fig. 1 Forest plot showing the fasting blood glucose at baseline comparing the metformin and control group based on fixed- and random-effect model, respectively

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Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interest.

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