Title: Many continuous variables should be analyzed using the relative scale: a case study of β2-agonists for preventing exercise-induced bronchoconstriction

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Reviewer: Wisit Kaewput

Reviewer's report:

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The title of the article is "Many continuous variables should be analyzed using the relative scale: a case study of β2-agonists for preventing exercise-induced bronchoconstriction".

Hemilä H, et al conducted a specific article types as "Methodology". This article aimed to compare relative vs absolute scale pooled outcomes using data from a recently published Cochrane systematic review that reported only absolute effects of inhalatory β2-agonists on exercise-induced decline in forced-expiratory volumes in 1 second (FEV1).

This is an interesting topic that can benefit from more thorough reporting and discussion, and appears to be well performed in general and the manuscript is well written. This topic will aid in understanding the usefulness of the relative scale and some limitation of the absolute scales in the estimation of the effects of β2-agonists on exercise-induced FEV1 decline. However, the manuscript still could be further improved after some revisions.

Specific comment;

In Methods section, Selection of the β2-agonists on EIB. The authors state that "One trial that was excluded by Bonini et al. on the basis that there was no clear diagnosis of EIB reported IPD for exercise-induced FEV1 decline and was included in our IPD analysis. Another trial with IPD data was identified through perusal of the reference lists in included RCTs, and was included in our analysis [29], but had not been identified by Bonini. Thus, a total of 14 trials reporting IPD data suitable for this analysis were identified (Table 1)". It must know what method for trials selection, before interpretation and compare the results from Bonini et al (in Discussion section). Please clarify what methods or inclusion and exclusion criterion for trials selection or study flow chart of the trials selection.

2. Please clarify how you manage the different confounding factors such as different type of bronchodilators, different duration between the β2-agonist administration and the exercise test, different baseline in an EIB study or in some case you using the pre-drug level as the baseline. Did you re-analyzed of sensitivity analysis or subgroup analysis?
3. In discussion section, please clarify, which cases did you prefer to use relative scale in limitation of relative scale?

4. In conclusion section, the author state "The absolute scale has been widely used in the analysis of FEV1 changes and it may have led to sub-optimal statistical analysis in some cases". There is an interesting point, please you clarify which cases that the outcome from "sub-optimal statistical analysis" can cause a clinical significant, in discussion part.

Thank you so much to let me having opportunity to work with this review.

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