Reviewer’s report

Title: Composite endpoints in degenerative disease: meta-analysis is over-analysis

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Reviewer: Qian H Li

Reviewer’s report:

The main issue of this paper is that the title of the paper does not appear to match the content. The title of the paper is “Composite endpoints in degenerative disease: meta-analysis is over-analysis”. However, the bulk of the paper is to show through mathematical derivation that the treatment effect over time (or different disease stages) of two composite endpoints may not necessarily be constant for the function decline in degenerative diseases, such as Alzheimer, while only one paragraph embedded in the discussion section covers the problems of the meta-analysis. The over-analysis claim of the meta-analysis is not sufficiently addressed in the paper. The only problems that the authors discussed in this paper are the potential problems of pooling patients together across disease severity. This reviewer believes that this paper needs to restructure so that the title and content will match.

This reviewer’s another major concern is that the problems addressed in this paper are not unique problems. The inconsistent treatment effect across disease severity does not necessarily exist only in composite endpoints. The inconsistent treatment effect is not only the problem of the degenerative disease. The problem of combining patients with different severity in meta-analysis is a generic problem of meta-analysis which is not unique to the degenerative disease and composite endpoints alone. The paper needs to re-focus the problems to increase its scientific value.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.