Reviewer's report

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

Version: 1 Date: 8 March 2011

Reviewer: Britta Tendal

Reviewer's report:

Major Compulsory Revisions

Overall
The authors highlight an important challenge with additive scales. I agree with the authors that additive scales may be problematic in individual trials especially if they have ceiling or floor effects. The authors’ suggestion of incorporating a scaling factor is interesting.

1) However I am not convinced that the methods and results presented in this study support the overall aim of the paper: ‘to address the impact of non-linearity of disease progression and construction of composite scales with regard to their impact on calculating effect sizes and performing meta-analyses.’ The mathematical reasoning in the paper, as far as I can see, only applies to calculation of effect sizes in individual trials. There are also no simulation studies to examine the effect on a meta-analysis level, neither is there any empirical evidence to back up the conclusion that ‘meta-analysis is over-analysis’.

2) I believe that the author’s should limit the discussion of the implications of performing meta-analyses based on additive scales to the discussion section where a more balanced discussion of the pro and cons of meta-analyses would be interesting. Meta-analyses may be useful as they can be used to see patterns that are unnoticed in the individual trials e.g. by a sensitivity analysis based on disease progress.

3) The title
“Composite endpoints in degenerative disease: meta-analysis is over-analysis” should be changed. Some readers of BMC Medical Research Methodology might mistake ‘composite endpoints’ as something different from a scale namely the occurrence of any event from among a given set of events after a certain period of follow-up. The last part of the title ‘meta-analysis is over-analysis’ should be deleted, as it isn’t supported by the results of the study. A suggestion for a different title: Additive scales in degenerative disease – introducing a scaling factor.

4) Abstract
Structure the abstract in sections: Background, Methods, Results and Conclusions
5) Introduction
Fourth paragraph: Although I see what is meant with ‘composite endpoints’, I think it would be more correct to talk about multidimensional scales (I assume that is what you mean).

6) Discussion
I do not believe that the methods and results support the conclusions regarding meta-analysis.

7) Discussion
The limitations of this study are not clearly stated.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests