Reviewer's report

Title: Evidence for placebo effects on physical but not on biochemical outcome parameters. A review of clinical trials

Version: 1  Date: 15 January 2007

Reviewer: Klaus Linde

Reviewer's report:

General
This is a very interesting paper on an important topic. The methodological approach is straightforward and adequate but, necessarily, not without problems. Selecting placebo-controlled trials of "stable" conditions for estimating the size of placebo effects (part 1) is difficult and cannot be made fully transparent within the space limits of a manuscript. Subgroup analysis of a published meta-analysis (part 2) also does not have perfect conclusiveness. These shortcomings are adequately discussed and difficult to avoid.

I have one fundamental point, but as this depends on my personal view of the "placebo problem" I have put this under discretionary revisions.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
None

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
- What is missing in the discussion are more detailed recommendations for future research. This paper is a good step in the direction of looking for reasons for the heterogeneity of placebo effects (see below).
- page 10: para 1 and para 2 - number of trials 26 vs. 29

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Discretionary Revisions (which the author can choose to ignore)

Personal, fundamental point: In my view the main merit of this paper is that it provides an empirical investigation of a plausible differentiating hypothesis (that placebo interventions are not the same for all outcomes) in an area where very heterogeneous things are often lumped together. What I do not like, however, is that the authors still seem to consider "placebo" as a homogeneous intervention (at least, this is suggested by terms such as "THE placebo phenomenon" or "placebo treatment"). In my view it is much more likely that "placebo effects" are a class of effects with a number of different mechanisms. Depending on the circumstances (patients, condition, interventions, outcome etc.) different mechanisms might be relevant. The concept of "THE placebo effect" might simply be nonsense. I would suggest to at least use terms such as "placebo phenomena" and "placebo interventions" which imply that there could be heterogeneity.

Minor point: page 11 - "In comparison to the pharmacological medication ... by on third - a remarkable efficacy". Frankly, I was surprised that it was ONLY one third, and that made me wonder about how reliable the primary studies are (unblinding etc).

Which journal?: Appropriate or potentially appropriate for BMC Medicine: an article of importance in its field

What next?: Accept for publication in BMC Medicine after minor essential revisions

Quality of written English: Acceptable

Statistical review: No

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