Reviewer’s report

Title: A review of clinical trial designs used to detect a disease-modifying effect of drug therapy in Alzheimer's disease and Parkinson's disease

Version: 0 Date: 19 Jan 2016

Reviewer: Lena Al-Khudairy

Reviewer's report:

Thank you for this review. my comments as following:

- Change the title to a review: line 2 and line 16 - search and data extraction was done by 1 reviewer and not 2 therefore a review is an appropriate title.

- line 9 (page 2) and line 11(page 4): can you please explain validity and what it refers to in your review.

- line 23 (page 3): please spell out AD.

- Methods (page 4): can you please mention your efforts in obtaining non published literature and were authors contacted?

- Study selection (page 5): can you please clearly state your inclusion criteria in terms of study design, population, intervention, comparison, outcomes. Clearly state what main points for exclusion.

- Data extraction (page 6): did you extract or assess sources of funding of RCTs? as this may introduce some bias.

- Methodological quality (page 6): you mention in your review that you will critique clinical trial designs therefore the assessment of the quality of included RCTs is necessary.

- Data synthesis (page 6): change to narratively synthesised.

- Results: please mention total number randomised.

- Results: please remove 20 to 26.

- Results: when referring to trials in your results please ensure you insert the reference of the trials mentioned (line 46). Please mention the number of studies when referring to study characteristics (line 46, line 14 page 8, line 34 page 8, line 32 page 11).

- Characteristics of participants (line 6): if you conducted any statistical analysis please mention the methods in your analysis section.
- Line 42 page 9: please spell out CSF
- Line 57 to 61: there is no need to constantly mention published and unpublished studies.
  
  Line 60 page 10: define long term follow up
- Results comments and recommendations: the results section is very lengthy and does not include quality assessment of included studies which is very important when assessing trials design. Recommend: condense the descriptive results and include methodological assessment of included trials and then discuss by trial design (as you already did in your discussion). Please mention within the text the (n) of study designs of included studies.
- Discussion: line 58 - 60 page 13: please rephrase.
- page 14 - end: when describing a trial design please insert reference.
- Flow diagram: please mention reasons of exclusion for others (n = 5)

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published
**Declaration of competing interests**

Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

i declare that I have no competing interests' below

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license ([http://creativecommons.org/licenses/by/4.0/](http://creativecommons.org/licenses/by/4.0/)). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal