Author's response to reviews

Title: Methodological quality of systematic reviews of animal studies: a survey of reviews of basic research.

Authors:

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Author's response to reviews: see over
**Reviewer #1: Peter Sandercock**

We thank reviewer’s support.

**Reviewer #2: Colin West**

1. The authors have nicely addressed the majority of all reviewers' comments. My suggestions below are generally minor, and are largely aimed at improving readability of the manuscript.

2. **Introduction:** change "became" to "become" in "... it has become clear ..."

3. **Methods:** change "tables" to "table" in "... used a random number table ...

4. **Discussion:** I agree with another reviewer that providing the statistical test comparing results with those of the Cochrane review paper (citation 14) is methodologically questionable. It would be better to report the raw numbers here, and remove the statistical test results. A statistical test across study results taken from very different methodologies is problematic. The raw numbers make your point clearly enough as it is.

5. **Discussion:** "The validity of our findings is inherent in the quality of our study." I am not sure what you are staying to say here, but the English isn't correct as it stands.

6. **Discussion:** "a priori" is two words.

7. **Discussion:** Write "... may have failed to capture ...

8. **Discussion:** "etc." is an abbreviation and needs a period.

9. **Discussion:** In the introduction, you may wish to add a sentence after the nimodipine example to clarify why this is important. For example, if the following sentence is true, it may clarify your arguments. "...nimodipine in humans,[10] Because the initial animal studies were not evaluated systematically, human trials of nimodipine proceeded at significant cost and potential human risk despite a lack of clear scientific rationale."

10. **Methods:** a comma may make the following sentence easier to read: "...latest publication for results, supplementing information ...

11. **Methods:** correct term is "... at a minimum ...

12. **Methods:** you may wish to add a comma to make the following sentence easier to read: "...
reviews of bench studies, defined as research ...

13. In Methods, the word "individually" does not seem necessary.
We modified this issue in the revised manuscript.

14. In Methods, the final sentence on power is not needed. I recognize this was added in response to another reviewer's comments, but it is obvious why your effect size was chosen, and unnecessary to further explain this. I would delete the sentence, "This estimation ... power of our study."
We agree with reviewer suggestion and we delete this sentence.

15. In Methods, write "divided into three domains".
We modified this issue in the revised manuscript.

16. In Methods, write "These items assessed ..."
We modified this issue in the revised manuscript.

17. In Methods, write "... level of significance was set at a=0.05 ..." (insert alpha symbol for a).
We modified this issue in the revised manuscript.

18. In Methods, write "Odds ratios and their ...", deleting "The".
We modified this issue in the revised manuscript.

19. In Results, write "... range of topics included ..." to match tense with previous sentence. Also add comma after "immunology".
We modified this issue in the revised manuscript.

20. In Discussion, write "... poor in their reporting ..."
We modified this issue in the revised manuscript.

21. In Discussion, make "Validity or quality ..." a new paragraph. Within this paragraph, change to "reviews we studied, increasing the risk of drawing erroneous inferences."
We modified this issue in the revised manuscript.

22. In Discussion, write "...basic research since these results ... clinical studies are undertaken."
We modified this issue in the revised manuscript.

23. In Discussion, write "...prerequisite before results are further tested in human clinical trials."
We modified this issue in the revised manuscript.

Reviewer #3: Maria Ospina
The review question is very relevant to the field; it is clear and explicitly stated. It emphasized the importance of exploring the quality of systematic reviews of animal studies, and the impact that this evidence may have to rationalize research in human subjects. The manuscript is clearly written in a concise manner. The search methods were comprehensive enough to locate studies relevant for the review. Appropriate databases were selected to identify the studies, and other potentially important sources were explored. The potential for publication bias was correctly addressed under the Discussion section. The inclusion criteria and study selection process was well documented. The methods of quality assessment are explicit, and the rationale for...
selecting a quality checklist over other methods available for evaluation of systematic reviews of human studies can be arguable, but the decision was documented and discussed. The review methods were documented in such a way that the work can be replicated by other reviewers. It also allows the review methods used to be subject to appraisal.

Ideally, the review process should involve independent assessment of studies relevance and quality. Please, clarify how many reviewers assessed the quality of the studies. When the authors said (Page 6) “One of us (LM) extracted data from the identified papers and a second reviewer (KSK) checked them for errors”, does it mean also that LM conducted QA and the QA results were verified by KSK?

We clarified this issue in the modified manuscript.

The authors presented both limitations and strengths of their research. I think it is important to highlight how their findings compare to reviews of research in humans, but I still consider that the reporting of p values for the indirect comparison between the results presented here and those from Jadad et al 1998 (e.g. p values for differences in proportions) is inappropriate as different methods (study selection, quality assessment of SRs) were used in the study reported here and the Jadad overview. I would suggest to mention how their findings compare to the Jadad overview, but avoid using the p values.

We removed the statistical test results from the revised manuscript.