Author's response to reviews

Title: Industry-supported meta-analyses compared with meta-analyses with non-profit or no support: Differences in methodological quality and conclusions

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Our comments on reviewers' reports

Referee: 1
Referee: Joel Lexchin

Major Compulsory Revisions

Joel Lexchin's comment: In the Conclusion the authors state that industry supported meta-analyses are less transparent than meta-analyses with other sources of funding or with no funding. However, at the beginning of the Discussion the claim is that industry supported reviews are methodologically inferior and this statement corresponds to the a priori hypothesis at the end of the Background section. The authors need to be consistent as to whether they are looking at methodologic quality or transparency. While it is likely that meta-analyses with poorer transparency will also be methodologically poorer, it is possible that methodologic quality may be the same even in the presence of different degrees of transparency. One reason why industry funded reviews might be less transparent is if they are published in lower quality journals that do not demand the degree of transparency that is found in higher quality journals. I would suggest that the authors examine the journal quality (perhaps measuring quality by the impact factor) where the different types of reviews were published to see if there is a difference.

Our comment: In the Discussion, Limitation section, we have now explained that this lack of details or transparency may lead to misjudgement of methodological quality.

Joel Lexchin's comment: The authors note that most of the nonsponsored meta-analyses and those with noncorporate sponsorship are Cochrane reviews and when the Cochrane reviews are excluded there is no difference in methodologic quality between the remaining reviews. Therefore, besides concluding that industry sponsored meta-analyses are of poorer quality an alternative interpretation could be that Cochrane reviews are methodologically superior to other meta-analyses regardless of sponsorship. The reference to references 16 and 17 in the Limitations (page 9) does not really address this issue. Furthermore, in looking at these two references I found the analysis of Cochrane reviews published in journals but no mention of “reviews based on the same methodological principles as Cochrane reviews.”

Our comment: We found that the median quality score was 6 for the 18 meta-analyses with non-profit or no support and 2.5 for the ten industry-supported meta-analyses (P < 0.01). When the Cochrane reviews were excluded the median quality score was 3 for meta-analyses with non-profit or no support and 2 for those with industry support (P = 0.06). Though the difference has changed, we believe that those with non-profit or no support are still of higher methodological quality compared to those with industry support. There is no good reason to interpret a p-value of 0.06 as being fundamentally differently from a p-value of 0.05. We have deleted “reviews based on the same methodological principles as Cochrane reviews.”
Minor Essential Revisions
Joel Lexchins comment:
Page 5:
In the Methods the authors state that they assessed the conclusions by looking at whether the experimental drug was recommended without reservations, with reservations or not recommended. However, in the Abstract they state that they used a binary scale. Did they combine two of the categories listed in the Methods section to create a binary scale?

Our comment: On page 5 we now make this more clear by using brackets: “…we judged the review authors’ conclusions by assessing whether the experimental intervention was recommended without reservations, or whether it was not recommended (or recommended with reservations)”.

Joel Lexchins comment:
Page 8, third paragraph:
It is not clear what the authors are referring to when they say that “the picture is similar” for trials. What “picture” do they mean?

Our comment: “On a trial basis the picture is similar” has been changed to “Studies of trials have found similar results.

Referee: 2
No referee 2

Referee: 3
Reviewer: Tom A Trikalinos

1. Consider clarifying that drugs vs. placebo meta-analyses were excluded (i.e., add ~7 words in the Methods).

Our comment: In the Methods, first section, we changed the phrase “Meta-analyses that we had authored ourselves were excluded” to “Meta-analyses that we had authored ourselves and meta-analyses of placebo controlled trials were excluded.”

2. Consider clarifying how you would classify the following scenario: "FUNDING: No specific funding was obtained for this research. [and then] ACKNOWLEDGMENT: Author XYZ acknowledges support by a career development award provided jointly by NIH and <DARK_SIDE/COMPANY_666>". I understand that this would be classified as industry-supported...

Our comment: In the Methods, Data analysis section, we changed the phrase “Industry support was defined as provision of grants, authorship, or other major assistance such as help with the statistical analysis” to “Industry support was defined as authorship, provision..."
of grants to the authors of the meta-analysis, or other major assistance such as help with the statistical analysis."

3. Building upon #2, consider mentioning in the discussion, limitations section, that the employed classification into industry-supported and so on is operational. In reality, specific projects classified as industry supported may have received quite different amount of actual industry support, ranging from none to extreme. I am not sure how often this is the case, nor whether the differences would be more pronounced if you had no misclassifications".

**Our comment:** In the Discussion, limitation section, we have now included “Our definition of industry support does not distinguish between different amounts of support, and our judgement of support is based on details reported in the meta-analyses. This can theoretically lead to misclassification of the support, as industry support may range from very little to generous, and details about some types of support may be lacking more often than others. However, the definition is operational and we believe that it includes the most important types of industry support."

4. Finally, in the 4/10 industry-supported meta-analyses that recommended the exp drug without reservations, was the industry manufacturing/selling the drug? What about in the other 6?

**Our comment:** Yes, in the 4 meta-analyses that recommended the exp drug without reservations, the supporting company was selling the drug of interest. Of those not recommending or only recommending the exp drug with reservations, the supporting company was selling the drug of interest in 3 cases, selling both drug of interest and control in 2 cases, and not selling any of the drugs in one. The following has been included in Results, Authors' conclusion section “The supporting companies of all 4 meta-analyses that were recommending the experimental drug without reservation were also selling the drug, but not the control drug. This only applied to 3 of the 6 industry supported meta-analyses that did not recommend or only recommended the experimental drug with reservations."