Reviewer's report

Title: Industry sponsorship and publication bias among animal studies evaluating the effects of statins on atherosclerosis and bone outcomes: a meta-analysis

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Reviewer: Gillian Currie

Reviewer's report:

This report refers to the manuscript ‘Industry sponsorship and publication bias among animal studies evaluating the effects of statins on atherosclerosis and bone outcomes: a meta-analysis.’

The aim of the study is clearly stated: “we examine whether there is evidence of publication bias in animal studies by expanding the previously performed systematic review and meta-analysis of statins and their effect on atherosclerosis outcomes to include an additional systematic review and meta-analysis of statins and their effects on bone outcomes.” The hypothesis and rationale are clearly stated “As a possible explanation for the larger efficacy estimates observed among non-industry sponsored studies, we hypothesize that publication bias is more evident in non-industry sponsored studies across various outcomes of interest.”

The methods are appropriate and have been used in other studies to assess for publication bias. My only reservation is the number of comparisons included in each subgroup analysis. The minimum number of comparisons that are generally used for these types of analyses in our group are 25 comparisons. It may be worth describing this limitation in more detail in the discussion section of the manuscript.

The data are sound however I recommend that the authors include more details on the number of comparisons included in each subgroup analysis.

The authors acknowledge that this work builds upon a previously published systematic review. However, the reference for this previous review needs to be corrected.

The title and abstract accurately convey what has been found.

The writing is of a high standard.

- Major Compulsory Revisions
  None

- Minor Essential Revisions

1. Background, fourth paragraph. “Collaborative Approach to Meta-Analysis and
Review of Animal Data in Experimental Studies” should read “Collaborative Approach to Meta-Analysis and Review of Animal Data from Experimental Studies”.

2. References, reference number 14 (Line 554). Spelling error. “CAMRADES” should read “CAMARADES”.

3. Background, fifth paragraph. “few registries of animal studies exist” the authors reference www.CAMARADES.info. A more specific reference would be useful?

4. Background, fifth paragraph. I cannot identify this statistic “most abstracts of animal studies (75%) submitted to a conference were never published” in the publication by Timmer et al. is referenced in the text. Can the authors clarify that this statistic is from this reference?

5. Methods, second paragraph. “For further details about inclusion and exclusion criteria, see our previous review [20].” This reference is the systematic review by Krauth et al. “Instruments for assessing risk of bias and other methodological criteria of published animal studies: a systematic review” but I’m not sure how the details on inclusion/exclusion criteria provided in this earlier review are relevant to the present review. Should reference 20 be the following publication: Nonindustry-Sponsored Preclinical Studies on Statins Yield Greater Efficacy Estimates Than Industry-Sponsored Studies: A Meta-Analysis. David Krauth, Andrew Anglemyer, Rose Philipps, Lisa Bero (2014) DOI: 10.1371/journal.pbio.1001770?

6. Methods, third paragraph. Should reference 20 be the above publication (Krauth et al. 2014)?

7. The title “Statistical Analysis- Publication Bias Assessments” should be in bold.

8. Results, first paragraph. The authors should state the number of atheroscleroris outcomes as they have done for the bone outcomes. E.g. We identified 49 unique studies evaluating x atherosclerosis outcomes in 3948 animals…”

9. Results, second paragraph. To avoid over-interpretation of non-significant results the final sentence should be changed to read “There was no significant difference in beneficial bone outcomes between industry sponsored (0.13; 95% CI -0.48, 0.73) and non-industry sponsored studies (0.48; 95% CI -0.10, 1.06) (p value= 0.41).

10. Results, third paragraph. It would be useful to include the number of comparisons for each subgroup (Atherosclerosis industry-sponsored/atherosclerosis non-industry sponsored/atherosclerosis no statement and the equivalent subgroups for bone outcomes).

11. Results, third paragraph. The first sentence should be changed to indicate how publication bias was assessed by the funnel plots e.g. Across all studies, (Figure 1; panels a, e) there appears to be publication bias in both
atherosclerosis and bone studies as assessed by funnel plot asymmetry.

12. Results, third paragraph. Please state how many comparisons are included in each funnel plot. It has been suggested for these types of publication bias analyses that you need at least 25 comparisons for the analysis to be sufficiently powered. There may not be enough comparisons to draw conclusions from funnel plots and trim and fill analysis.

13. Results, fourth paragraph. Similarly, we would recommend a minimum number of 25 comparisons for Egger’s regression.

14. Discussion, second paragraph. Extra full stop in second last sentence.

15. Discussion, sixth paragraph. The authors state “reporting has improved slightly since the publication of ARRIVE guidelines.” Is there any evidence to support this? We would expect reporting to improve since the introduction of ARRIVE but I do not know if this has been observed.

Discretionary Revisions

1. Methods, fifth paragraph. The authors calculated the effect of statins using a standardised mean difference (SMD) for each outcome and pooled using a random-effects model. The authors state the null hypothesis and the meaning of a negative or positive value. I suggest that the wording of “that the statin increases the risk of atherosclerosis harms outcomes or beneficial bone outcomes when compared to control or placebo” should be changed to “that the statin increases the risk of atherosclerosis outcomes or increases the likelihood of beneficial bone outcomes when compared to control or placebo.” Similarly, I suggest the converse description should be changed to “that the statin reduces the risk of atherosclerosis outcomes or reduces the likelihood of beneficial bone outcomes when compared to control or placebo.”

2. The study by Riet and colleagues appears to contradict the findings of the present study. Riet et al. report that only 10% of for-profit research would be published whereas 80% of non-industry sponsored research would be published. However, the present study identified potential evidence of publication bias to be more prominent in non-industry sponsored studies. Perhaps discuss the potential reasons for the different findings.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.