Author’s response to reviews

Title: Professional medical writing support and the quality, ethics and timeliness of clinical trial reporting: a systematic review

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Version: 1 Date: 17 May 2019

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Professor Joerg Meerpohl

Editor, Research Integrity and Peer Review

17 May 2019

Dear Professor Meerpohl,

On behalf of my co-authors, I would like to thank you for your review of our manuscript "Professional medical writing support and the quality, ethics and timeliness of clinical trial reporting: a systematic review" (RIPR-D-18-00030). The reviewers’ insights on our manuscript were very helpful and we have revised the manuscript to incorporate almost all of their suggested changes. Please find below our responses to each comment.
Evaluation from reviewer 1

Abstract: The conclusion given in the abstract conclusion sounds a little too straightforward, given the results presented in the review. The statement that the "overall quality" increases would certainly benefit from a bit more empirical evidence. Maybe you could choose a wording that is more careful, as you do for instance by stating that PMWS "may improve the timeliness of publication". The wording on Page 7 lines 151-53 also sounds more appropriate.

Response: We have amended this statement in the conclusion section in the abstract, replacing ‘increases’ with ‘is positively associated with measures of…’

Background: I think the background could benefit from some few more words on why the timely publication of trial results is an ethical imperative. I would therefore suggest to link this study in the broader context of the "Value and waste"-debate (see for instance Macleod MR, Michie S, Roberts I, et al.: Biomedical research: increasing value, reducing waste. Lancet. 2014; 383(9912). There are currently many initiatives and research groups working on improvement of trials results reporting, some of them are already cited. It would underline the importance of this systematic review.

Response: We have amended the first sentence to highlight the waste reduction element of timely reporting and included a reference to Moher et al, 2016 (Increasing value and reducing waste in biomedical research).

Methods: Is there a reason why you limited the supplementary searches from 2014-17

Response: Supplementary searches were limited to focus on the most recent congresses and keep the workload manageable for this manual element of the search strategy. Supplementary searches of the previous 3-4 years is generally considered reasonable for systematic reviews. Additionally, the supplementary searches were carried out alongside the main searches on 8 March 2018. The manuscript has been amended accordingly.

Methods: Overall, it is not entirely clear how you define quality, ethics and timeliness. How did you extract information from the included studies on e.g. ethics? What would have been ethical aspects? As your results suggest, the only issue in "ethics of publication" is the reporting of non-pre-specified outcomes. How is this distinct from quality (e.g. the CONSORT items)? If you were not able to pre-define what you have been looking for when you searched for "ethics of publication", I would suggest to omit "ethics" as an individual result, but instead subsume the of non-pre-specified outcomes to "quality". To me, even adherence to CONSORT is part of an
"ethics of publication". Later in the conclusions section, however, you list some more ethical issues (e.g. transparency on conflict of interest etc.) and you cite two studies. Why have these studies not been included in your review?

Response: For the protocol of this study, we considered ‘quality’ as overall completeness of reporting. We agree that quality reporting and timely dissemination of clinical trial results are an ethical imperative. Although quality, ethics and timeliness are semantically distinct outcomes, it can be difficult to objectively separate quality and ethics with regards to research reporting. As such, we have combined the quality and ethics results in one section entitled ‘quality and ethics of reporting’. However, we think that ‘timeliness’ is a distinct outcome that should be kept separate.

The two ‘ethics’ studies described in discussion (Desai et al (2017) and Woolley et al (2011)), were not focused on studies reporting clinical trial outcomes and as such, did not fit the inclusion criteria for this systematic review.

Methods: Page 4, line 93: I would suggest to say "effect" instead of "influence", as the latter is too causal.

Response: We have made this amendment

Results: The results are presented in a nice and readable manner. Only point is the unclear operationalisation of "ethics of publication". However, I wonder if in any of the reviewed studies the authors also investigated how quality of reporting with or without PMWS differs in relation to study characteristics (e.g. phase I/II versus phase III trials). Is there any evidence on this?

Response: We agree that this is an interesting question and could be the focus of a further study. However, none of the included studies separated RCTs by phase. Additionally, variations in quality of reporting with study characteristics was beyond the scope of this study and has such has not been discussed.

As mentioned earlier, we have combined the quality and ethics results in one section in line with their overlapping definitions.

Evaluation from reviewer 2
Background: Woolley (7) was 6%; Kim (10) was 11-18%; Nastasee (11) was 5.1-11.3%, so 5–18% perhaps? Shame there isn't anything post-GPP-3...

Response: We thank the reviewer for suggesting a range more reflective of the cited studies. We have amended the statement accordingly.

Methods: Were there no suitable contributions from the AMWA journal, or didn't you look? I think you should mention AMWA either way.

Response: The focus of the supplementary searches was on ISMPP congress proceedings and the journals Medical Writing and The Write Stuff (which are available via the EMWA website). Searching the AMWA journal was not part of the search strategy. We have now mentioned this in the manuscript.

Results [previously lines 99–100, currently lines 101–103]: Can you switch this sentence around? You only got to exclude 70 after adding these 3 to the 67 exclusions from your title/abstract screen. Took me a while to reconcile this sentence with Figure

Response: This sentence has been amended to clarify the study inclusion and exclusion process

Results [previously lines 111–112, currently line 115]: These two citations are the same study. Is it fair to use both the abstract and publication?

Response: Although this finding was reported in the congress abstract and full publication, the p-value was reported in the congress abstract only.

Results [previously line 130, currently line 132]: Same comment as above. Is it fair to cite both the abstract and the publication?

Response: Similarly, the p-values for these findings were reported in the congress abstract only.

Conclusions [previously line 162, currently lines 163–164]: Would you like to speculate on why this may be? Arguments may include word count constraints, desire to get the key results in the abstract at the expense of methodology...?
Response: We have added an explanation of why adherence to CONSORT-A may be affected by word-count constraints.

Conclusions [previously line 190, currently lines 192–194]: Again, would you like to speculate on potential reasons for this? Do you think that industry-sponsored research (as indicated by the use of PMWS) undergoes more intense scrutiny by peer reviewers? There are some studies to support this view (Lippert et al. Perceptions of conflict of interest disclosures among peer reviewers. PLoS ONE 2011; 6(11): e26900) and Kesselheim et al. A randomized study of how physicians interpret research funding disclosures. N Engl J Med. 2012;367(12):1119–27) though the latter is indirect.

Response: We have added a sentence to the discussion outlining the possible influence of industry funding on peer reviewers’ attitudes.

Conclusions [previously line 196, currently line 201]: Is quantity a fair indicator? There are, of course, overly prolific authors (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4548528/) Is there a danger of implying that PMWS can contribute to inappropriately prolific authorship?

Response: Although this is an interesting question, the results of the current study show a positive effect of PMWS on timeliness and quality/ethics of publication, including adherence to CONSORT and publication guidelines. By specializing in preparation of clinical trial publications, professional medical writers are well placed to aid in the rapid dissemination of trial findings under the direction of the authors. This suggests that PMWS may improve overall publication rates; it is important to note that the role of PMWS is subject to strict publication guidelines that should prevent inappropriately prolific authorship from clinicians who work with PMWS.

Conclusions [previously line 230, currently line 235]: Thank you for mentioning this important point. Rather self-servingly (!) there is a similar analysis of the European ISMPP meeting output, though it has remained a preprint (https://peerj.com/preprints/2499/)

Response: We thank the reviewer for informing us of this replication study. We have added the citation accordingly.

Conclusions [previously line 239, currently line 244]: You're implying that you're talking about two different surveys here, but are only citing one publication. I think you mean the Camby study for this 90% stat (Camby, I., Delpire, V., Rouxhet, L., Morel, T., Vanderlinden, C., Van
Driessche, N., & Poplazarova, T. (2014). Publication practices and standards: recommendations from GSK Vaccines’ author survey. Trials, 15(1), 446.). However, I notice that reference 36 (the authors’ own poster) has gone uncited... along with references 37 and 38... (however I just found ref 36 in the acknowledgements)

Response: We thank the reviewer for noticing the non-citation of the Camby et al study in error. We have updated this citation accordingly.

Hopewell et al, 2014 (previously reference 37, now 41) and Hays et al, 2016 (previously reference 38, now 42) are cited in Table 1.

Based on the helpful reviewer comments, we have updated the manuscript accordingly. We hope that this manuscript meets the high standards of Research Integrity and Peer Review and is now acceptable for publication.

We look forward to hearing from you.

Yours sincerely,

Obaro Evuarherhe