Author’s response to reviews

Title: Reproducibility of Clinical Research in Critical Care: A Scoping Review

Authors:

Daniel Niven (daniel.niven@albertahealthservices.ca)
Jared McCormick (tjmccmick@gmail.com)
Sharon Straus (sharon.straus@utoronto.ca)
Brenda Hemmelgarn (brenda.hemmelgarn@ahs.ca)
Lianne Jeffs (jeffsl@smh.ca)
Tavish Barnes (tavish.barnes@ahs.ca)
Henry Stelfox (tstelfox@ucalgary.ca)

Version: 2 Date: 11 Jan 2018

Author’s response to reviews:

January 11, 2018

Alessandro Recchioni

Associate Editor, BMC Medicine

RE: Reproducibility of Clinical Research in Critical Care: A Scoping Review

Dear Editor Recchioni:

Thank you for the opportunity to revise our above-named manuscript. Our response to concerns raised by reviewers is outlined below. Changes appear highlighted in yellow within the revised manuscript.

We hope you find these revisions acceptable and look forward to your response.
Yours truly,

Daniel J. Niven
MD, MSc, PhD, FRCPC

Reviewer Comments

Reviewer #1.

We thank the reviewer for their kind review of our revised manuscript.

Reviewer #2:

1. Inclusion of systematic reviews, and systematic reviews with meta-analysis in the scoping review. “They persist in lumping together RCTs and systematic reviews with and without meta-analysis. The reproducibility of SRs is quite a different topic. The data points in SRs are the outcomes of RCTs, not individual patient data. And the overlap of publications between primary SRs and its replication attempt will be large, unlike the overlap in data between the RCTs you compare. Thus replications of SRs are re-analyses of the same data mainly, and not the retest or approximately reproducibility attempts the authors claim them to be. So my advice would be to remove the SRs from the data set.”

Response: We have excluded all systematic reviews and systematic reviews with meta-analyses from the scoping review. This change is reflected in every section of the manuscript. All data displays have been modified accordingly. Because the published protocol (BMJ Open 2015;5:e008244) described inclusion of systematic reviews and meta-analyses, we included a sentence in the methods indicating the reason why the results reported in the manuscript differ from those predicted from the published protocol. This sentence can be revised as necessary.

Page 6, lines 6-9: “The published protocol indicates intention to include systematic reviews, systematic reviews with meta-analyses, and studies examining the clinical effects of diagnostic interventions within the target cohort of articles, however, at the request of the Journal, these studies were removed from this manuscript.”

Inclusion of each of the other modifications relevant to exclusion of systematic reviews and meta-analyses within this letter was not feasible as they occurred in nearly every section of the manuscript. Thus we refer editors and the reviewer to the revised manuscript where each change is highlighted in yellow.
2. Inclusion of studies examining the effects of diagnostic tests in the scoping review. “I can still not understand why also RCTs on diagnostic interventions were included while excluding the very large majority of non-randomized diagnostic accuracy studies. Combining data on the reproducibility of therapeutic and diagnostic RCTs makes very little sense to me. An analysis of the reproducibility of both randomized and non-randomized diagnostic accuracy studies would be really informative and seems to deserve a separate article. Consequently I would strongly advise to remove the diagnostic RCTs from the data set for the current publication.”

Response: Similar to revisions excluding systematic reviews, we have excluded all studies examining the effects of diagnostic tests from the scoping review. This change is reflected in every section of the manuscript. All data displays have been modified accordingly. Because the published protocol (BMJ Open 2015;5:e008244) described inclusion of studies examining diagnostic tests, we included a sentence in the methods indicating the reason why the results reported in the manuscript differ from those predicted from the published protocol. This sentence can be revised as necessary.

Page 6, lines 6-9: “The published protocol indicates intention to include systematic reviews, systematic reviews with meta-analyses, and studies examining the clinical effects of diagnostic interventions within the target cohort of articles, however, at the request of the Journal, these studies were removed from this manuscript.”

Inclusion of each of the other modifications relevant to exclusion of systematic reviews and meta-analyses within this letter was not feasible as they occurred in nearly every section of the manuscript. Thus we refer editors and the reviewer to the revised manuscript where each change is highlighted in yellow.

3. Interpretation of the effects of publication bias on reproducibility. “The authors do not seem to understand why I was so surprised that they do not mention non-publication (publication bias) and selective publication (outcome reporting bias or 'cherry picking’) as the likely most important cause of lack of reproducibility. They argue that they focus on high quality reproducibility attempts in high impact journals and say that's improbable that such studies would suffer from publication bias. But that was not my point at all. My remark concerned the initial publications. It's quite likely that these are the 'tip of the iceberg' and are for a large proportion the result from publication bias and (outcome) reporting bias. Both biases lead to an exaggerated positive picture in the public track record. One should not be surprised at all that these effects partly disappear or diminish on replication.”
Response: The way in which the reviewer currently frames their view on the effect of publication bias on our results has made their point clearer. It appears the reviewer is suggesting that through focus on high impact literature, original studies included in our study may have been published based on the high-profile nature of the intervention examined, and results obtained, and owing to these biases, are more likely to report results that are not reproducible. While this is certainly possible, our results (i.e. rate of reproduction attempt and reproducibility) compare favourably with other studies examining the reproducibility of clinical research, including those that focused on potentially lower-profile literature. We have thus softened our statement that mitigates the potential consequences of focusing our study on high-profile literature.

Page 13, lines 22: “Restricting the primary search to high-profile literature may have overestimated the number of practices with a reproduction attempt. However, through identification of 158 clinical critical care practices, and reporting the estimate of reproduction attempts at the level of the practice rather than the individual original study, it’s less likely that inclusion of potentially lower profile literature within the primary search would considerably alter this estimate.”