Author’s response to reviews

Title: Hospital volume-outcome relationship in total knee arthroplasty: protocol for a systematic review and non-linear dose-response meta-analysis

Authors:
Tanja Rombey (tanja.rombey@uni-wh.de)
Käthe Gooßen (kaethe.goossen@uni-wh.de)
Jessica Breuing (jessica.breuing@uni-wh.de)
Tim Mathes (tim.mathes@uni-wh.de)
Simone Hess (simone.hess@uni-wh.de)
Rene Burchard (rene.burchard@uni-wh.de)
Dawid Pieper (dawid.pieper@uni-wh.de)

Version: 2 Date: 03 Feb 2020

Author’s response to reviews:

Dear Dr Malic,

We wish to thank you and the reviewers for re-considering our manuscript "Hospital volume-outcome relationship in total knee arthroplasty: protocol for a systematic review and non-linear dose-response meta-analysis" (SYSR-D-19-00161R1). We addressed the comments of reviewer #3, which were very helpful in further developing our protocol.

In addition, we updated the affiliation of one author (RB).
We confirm that all author details on the revised version are correct, that all authors have agreed to authorship and order of authorship for this manuscript and that all authors have the appropriate permissions and rights to the reported data.

Best wishes on behalf of all authors,
Tanja Rombey

Reviewer reports:
Reviewer #2: As all my comments were properly addressed and resolved, I recommend this manuscript for publication.

AUTHOR RESPONSE: Thank you very much for reviewing our manuscript again!

Reviewer #3: This is a very well-written protocol, and I commend the authors on the comprehensive and rigorous manuscript they have prepared.
AUTHOR RESPONSE: Thank you very much for reviewing our manuscript!

1. Typo on page 10, line 326 - the R package referred to is metafor. It has been misspelled it as 'metaphor'.

AUTHOR RESPONSE: Thank you for pointing this out! We have corrected the typo now.

CHANGES TO THE MANUSCRIPT: Ll. 322 (clean version): “All analyses will be performed with R using the metafor and dosresmeta packages (40, 41).”

2. I believe the section on 'Meta-bias(es)' (page 10, lines 328-329) can be expanded upon. The authors have comprehensively incorporated into their protocol rigorous non-statistical methods of reducing publication bias, e.g. searching clinical trial registers, contacting experts in the field, and searching for conference abstracts. The use of more than one statistical test to assess publication bias is also prudent as it prevents over-reliance on a single measure, and a more liberal p-value of &lt;0.1 has been chosen which will further reduce the risk of false negatives.
   - The authors could expand upon this section by further substantiating their decision to approach publication bias in this way, and may find the following paper helpful: Lin L, Chu H, Murad MH, Hong C, Qu Z, Cole SR, Chen Y. Empirical comparison of publication bias tests in meta-analysis. Journal of general internal medicine. 2018 Aug 1;33(8):1260-7.
   - It is also worth noting that, according to the Cochrane Handbook section 10.4.3.1, "tests for funnel plot asymmetry should only be used when there are at least 10 studies included in the meta-analysis" (Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org.). I believe referencing this will strengthen this section of the paper.

AUTHOR RESPONSE: We fully agree with you! We have further elaborated on our methods regarding the assessment of meta-biases including the suggested references. In place of the Cochrane Handbook, we cited the reference that was cited in the respective chapter of the Cochrane Handbook, namely: Sterne JAC, Sutton AJ, Ioannidis JPA, et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ. 2011;343:d4002)

CHANGES TO THE MANUSCRIPT: Ll. 324-330 (clean version): “For the univariate inverse-variance random-effects meta-analysis, we will assess publication bias by visually inspecting funnel plots for asymmetry. Following the recommendations by Sterne et al. (42), we will only test for funnel plot asymmetry in meta-analyses including at least 10 studies. As empirical research found that agreement between different tests of publication bias is relatively low (43), we will apply two tests, namely Egger’s test (44) and Begg’s test (45). A p-value &lt;0.1 will be considered statistically significant because the statistical power of the publication bias tests is generally low (44, 45).”

3. Page 10, line 326 - the R package 'meta' (Balduzzi S, Rücker G, Schwarzer G (2019). "How to perform a meta-analysis with R: a practical tutorial." Evidence-Based Mental Health.) can be helpful in calculating pooled estimates, as the authors state is their plan on page 9 (lines 305-307), when pooling effect estimates using the generic inverse-variance method. It might be worth including this in the given list of R packages.

AUTHOR RESPONSE: Thank you, but the planned analysis can also be performed using the metafor package, therefore we decided to not add the meta package to the given list of R packages.
As a general comment, I believe the scope of this research extends beyond Germany and Europe. I understand the research team has a specific focus-group project outlined to facilitate the advancement of policy change in Germany as a result of this study, but given that the included literature is from all over the world, readers could potentially apply the findings to their own healthcare settings outside of Germany. This might be worth mentioning.

AUTHOR RESPONSE: We agree with you and have added a paragraph on this matter at the beginning of the discussion section.

CHANGES TO THE MANUSCRIPT: Ll. 365-367 (clean version): “With this systematic review we aim to inform future health policy decisions in Germany. As we will include studies dealing with populations from any country and continent, it is likely that our findings will also be applicable to healthcare settings outside Germany and Europe.”