Reviewer’s report

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

Version: 0 Date: 19 Jul 2019

Reviewer: Mark Rockley

Reviewer's report:

This is a well written protocol, and the study is nicely justified in the introduction. I appreciate that the reported data will likely be represented by incomplete or heterogeneous reporting standards, and this will naturally limit the conduct and interpretation of analysis. While the study question is valid, I am concerned that the quality of available reported evidence will limit analysis and interpretation, and encourage caution in interpreting the final results.

Questions:

Is there a specific primary "patient-relevant outcome"?

Inclusion criteria: If I am interpreting your study correctly, I would clarify that included studies need to report not just at least two hospital volumes, but also report the specific outcomes associated with each center.

Inclusion of studies reporting revision TKA: Would this not confound outcomes such as readmission rate and implant survival?

Variables: Do you believe that the surgeon volume is relevant and potentially co-linear with hospital volume? If reported, surgeon volume and years of experience would likely also be relevant factors to record in light of the study's question regarding hospital volume. I would explicitly define surgeon volume and experience in the "Surgeon Characteristics" variable.

Please define TKA implant survival.

You state that the methodological approach is multivariate meta-regression. Please expand on the 'multivariate' term. Are you referring to using the multivariate adjusted estimates from each study (assuming that most studies will include different variables in their respective reported models), or are you performing the multivariate regression by actively including study variables (eg: year of publication)? If the former, are there specific variables included in the model that are required for inclusion in analysis? If the later, what is the model selection process?

Standardizing hospital volume: As you point out, this assumes a constant volume-outcome effect, however it also assumes a constant outcome rate. Some of your potentially expected outcomes (eg: surgical site infection) will have a heavily skewed postoperative outcome rate soon after surgery, and is expected to be very rare more than a year post-operatively. I am not convinced that your justification of the high volume and long history of this procedure will address this issue, as it is the inherent pattern
of postoperative complications. Furthermore, the binary post-operative complication variables and QOL variables need to be treated differently in this standardization process.

As an aside comment, I would also suggest that this could be a situation where inclusion of RCTs may actually introduce a differential bias, as they often require minimum hospital and/or surgeon volumes for participation. Therefore, it is foreseeable that lower-volume reports are represented by cohort studies, while higher-volume reports are more represented by RCTs.

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