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: 23 Jul 2019

Reviewer: Stefan Sauerland

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As volume-outcome relationships are increasingly important to structure healthcare, this protocol for a systematic review addresses an interesting topic. The planned analysis has several strengths:

1) A big advantage of the proposed review will be the non-linear modelling. The literature has produced conflicting results on the volume-outcome relationship in total knee arthroplasty (TKA), and the most recent studies have further contributed to this puzzling situation (see for example Arias-de la Torre et al., J Clin Med 2019 pre-published online https://www.ncbi.nlm.nih.gov/pubmed/31086009).

2) As no systematic review has examined volume-outcome relationships in TKA since 2012 (Critchley et al.; Knee 2012; 19: 513-8), it is worthwhile to perform an update of these previous, but now outdated systematic reviews.

3) The involvement of patients by meeting them in focus groups is certainly a major laudable asset of the current proposal.

On the other hand, the authors propose very detailed and time-consuming methods, some of which may not be necessary:

4) Hand-searching of conference abstracts (line 170 to 177) should be omitted, because the scientific usability and credibility of such preliminary and superficial reports will be insufficient for the planned analyses. Moreover, inclusion of conference abstracts will neither improve the results of the systematic review nor remedy possible publication bias.

5) The use of ROBINS-I (line 248) has turned out to be difficult (Minozzi et al. J Clin Epidemiol 2019; 112: 28-35). In the proposed systematic review, it would probably be sufficient to focus only on two or three main aspects of risk of bias, e.g. availability of data on confounding variables, pre-specified analyses, etc.. Other aspects such as the measurement of exposures and outcomes are less relevant in volume-outcome studies, since most variables can be recorded with very high validity and reliability. There are two additional comments on the foreseeable shortcomings of the review:

6) The planned analyses are restricted to studies reporting hospital rather than surgeon volumes. This methodological aspect should be discussed in more detail, because several studies found that surgeon

7) In line 235, "early revision rate" is defined as the primary outcome. Will this "early" period of time require an exact definition? Furthermore, it might be helpful to exclude studies due to insufficient length of follow-up (e.g. studies limited to hospital data).

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