**Reviewer’s report**

**Title:** The Efficacy of Multiple versus Single Hyaluronic Acid Injections: A Systematic Review and Meta-Analysis

**Version:** 0  **Date:** 24 Aug 2017

**Reviewer:** Charlotte Beaudart

**Reviewer's report:**

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The efficacy of multiple versus single hyaluronic acid injections: a SR and MA.

**Major review.**

- Authors should follow the PRISMA statement for SR and MA.
- Authors should indicate the exact date on which the search strategy has been applied on the databases.
- The reviewer does not understand the difference between MEDLINE and Pubmed databases.
- Did the authors search the grey literature or unpublished literature? If not, this should be reported as a weakness of the study.
- Authors should report additional information on the methodology regarding the study selection. In figure 1 it is clear that study selection was performed on 3 stages but no information in given in methods.
- Did the authors contact authors of individual studies in case of missing data?
- Quality of individual studies should be assessed by 2 authors, independently. There are validated tools to assess quality of RCT. Please use one of them.
- Table 1 should specify which one of the different studies is funded by industry.
- Data extraction has been done by only 1 reviewer. This is a weakness and not recommended for MA. Another independent reviewer should check all extracted information to ensure quality of the reporting.
- Authors should use random effect models instead of fixed effect models. Indeed, if heterogeneity is observed in results (which is the case in several of the MA), random model should be used.
- Authors should assess publication bias.
- Authors should investigate the source of heterogeneity in their results.
- Authors should perform sensitivity analyses by deleting one study at a time. With this method, they make sure that results are not influenced by one single study.
- It is unacceptable to combine results of two or less studies in a MA. Ideally, at least 10 individual studies should be combined to offer a valuable MA. Moreover, the purpose of the paper is to assess efficacy of multiple versus single injection. Figures do not report that.
- Figure IV and V are not readable, should not include "not estimate" data and should be removed from the manuscript.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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Acceptable
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