Reviewer’s report

**Title:** Differential methylation in rare ophthalmic disorders: a systematic review protocol.

**Version:** 1  **Date:** 14 Jan 2019

**Reviewer:** Sebastien Kenmoe

**Reviewer's report:**

I have reviewed the revised version of the manuscript and it is much improved. However there are some points which I feel still require clarification.

Comment: Line 168. Specify the software that will be used.
Response: We searched MEDLINE using the Ovid platform. Could the reviewer please clarify which software they are referring to if not this?
Action taken: We have now specified MEDLINE via Ovid in our methods section.

Reviewer response: Sorry, the misunderstanding about this was related to a typo. It was to specify the software that will be used for the reference management, which is located at line 186 and not 168.

Line 111 to 113 seems to be generally not important. To match the PICO statement, methylation could be seen here as an exposure rather than an intervention. I suggest this part to be removed.

Line 135, Why not consider common eye diseases and/or normal patients as comparator for this study as indicated in the other parts of the manuscript?

The subheadings included from line 115 to 144 are confusing. As an example, the text supporting "context" subheading does not seem appropriate. I recommend the authors to remove all these subheadings and leave all the information in this part with the subheading "inclusion criteria". Especially since the recommendations to the authors of the Systematic Review Journal do not require these subheadings.

What about publication bias? I would suggest author to plan assessing the asymmetry of the funnel plots or by doing a test such as Egger's test in data analysis. Author could also plan to use a sensitive/correction analysis in the cases of publication bias?

**Level of interest**

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