I. LIST OF ITEMS TO INCLUDE WHEN PROPOSING AND SUBMITTING A SYSTEMATIC REVIEW AND META-ANALYSIS OF MEDICAL LITERATURE

If you would like to publish a systematic review/meta-analysis in the *American Journal of Ophthalmology* (AJO), you must first complete a proposal using this document. This proposal must include the proposal parts of the following sections below: A, B, C, D, F2, and G. This proposal MUST be written and submitted to the AJO for approval before the systematic literature search for the systematic review/meta-analysis is conducted. Therefore, the AJO will not consider a systematic review/meta-analysis manuscript that has already been completed or rejected by another journal. The only exception to this would be if there was a protocol that had been pre-approved by the Cochrane Collaboration.

If the proposal is approved, the systematic review/meta-analysis manuscript submission to the AJO must be accompanied by this document with ALL sections below completed. This completed document must be submitted in addition to the manuscript. All of the text that was in the original proposal MUST appear in the completed version of this document that accompanies manuscript submission, with any changes (and/or additions/deletions) from what was in the original proposal, in the appropriate places.

All of the information required for a systematic review/meta-analysis must be included in the manuscript. Due to space constraints and word limitations, authors will need to include much of this information in online supplements. Generally, when the manuscript includes both a systematic review and a meta-analysis, the AJO prefers to have the meta-analysis presented in the print version of the article, and the systematic review and any additional material included in online supplements. The Introduction to the meta-analysis would refer to this online supplemental systematic review of the literature.


A. TITLE

1. Title:

   a. **AJO instructions:** Identify the manuscript as a systematic review, a meta-analysis, or systematic review and meta-analysis. The AJO will consider publishing a systematic review with or without a meta-analysis. The AJO will
consider a systematic review without a meta-analysis only if the articles identified in the systematic literature search preclude a meta-analysis. That is, if after performing the systematic review, a meta-analysis of the data is determined to be infeasible. (See Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to Meta-Analysis. 2009 Chichester, UK: John Wiley & Sons, Ltd. Chapter 40). Therefore, all proposals for a systematic review must include a proposed meta-analysis, since it is impossible to know, in advance, whether a meta-analysis will be feasible. The AJO will consider a meta-analysis without a systematic review, but only if the meta-analysis is based on a systematic and comprehensive search of the literature, so no proposal for a meta-analysis without a systematic and comprehensive search of the literature will be considered.

2. List the authors
   a. AJO instructions: The authors must assert that the systematic literature search for the manuscript was not begun prior to submission of the proposal. Any changes to the authors (after proposal approval) requires prior approval by AJO.

B. ABSTRACT
   1. The proposal’s preliminary abstract must include the sections relevant to the Introduction and Methods.
   2. Manuscript: complete structured summary

C. INTRODUCTION
   1. Rationale
      a. Proposal (planned)
      b. Manuscript (changes from proposal only)
   2. Objectives:
      a. Proposal (planned)
      1) AJO instructions: Reporting of Objectives must include the items listed under “Reporting of background” in the table of the MOOSE document.
      b. Manuscript (changes from proposal only)
      1) AJO instructions: The manuscript introduction should be similar in length and scope to an Introduction for an Original Research Article (see http://www.elsevier.com/journals/american-journal-of-ophthalmology/0002-9394/guide-for-authors).

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D. METHODS and RESULTS (See Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to Meta-Analysis. 2009 Chichester, UK: John Wiley & Sons, Ltd.)

1. Protocol and registration:
   a. Proposal (planned)
   b. Manuscript (changes from proposal only)

2. Eligibility criteria:
   a. Proposal (planned)
      1) AJO instructions: Each inclusion and exclusion criterion must be described, explained, and justified. The AJO will not consider any proposal with overly restrictive inclusion and exclusion criteria. To avoid introducing bias into the medical literature, the AJO requires systematic reviews and meta-analyses to be of the complete literature on a topic, with subgroup analyses (usually included in the same publication as the comprehensive systematic review and meta-analysis) for subsets of articles that meet more restrictive inclusion and exclusion criteria (including those for subgroups based on study design).
   b. Manuscript (changes from proposal only)
      1) AJO instructions: Changes to inclusion/ exclusion criteria (at the time of the manuscript submission) will not be viewed favorably, without a clearly compelling rationale. Therefore, if this is necessary after proposal approval, re-approval should be sought before the manuscript is completed and submitted.

3. Information sources:
   a. Proposal (planned)
      1) AJO instructions: Information sources should include (but are not limited to) all applicable electronic databases, all relevant articles in the reference list of any relevant article, and all relevant articles which cite any relevant article.
   b. Manuscript (changes from proposal only)

4. Search:
   a. Proposal (planned)
      1) AJO instructions: All limits should be described and explained (e.g. exclusion of non–English-language citations), and these must be consistent with the inclusion and exclusion criteria described above. Reporting of the planned search strategy must include how the authors plan to provide all items listed
in this section of the table in the MOOSE document. Also describe any planned contact or attempted contact with authors of published and/or unpublished research.

b. Manuscript (changes from proposal only)

1) AJO instructions: The dates for all searches must be provided and these must be after the date that the proposal received approval from the AJO.

5. Study selection:

a. Proposal (planned)

1) AJO instructions: Study selection is one of the most critical elements in a systematic review and meta-analysis so the authors must attempt to reduce/eliminate potential bias.

b. Manuscript (changes from proposal only)

1) AJO instructions: This must include a flow diagram of the article selection process with reasons for and numbers of exclusions at each stage. (See Vanner EA & Stewart MW. (2011) A Systematic Review / Meta-Analysis of the Effects of the Timing of Pars Plana Vitrectomy for Removal of Intravitreal Retained Lens Fragments after Surgery for Age-Related Cataracts. American Journal of Ophthalmology 152(3), 345-351.e3 PMID: 21683330. Figure 1 for an example.) The flow diagram must be adapted for each systematic review and meta-analysis.

2) AJO instructions: The authors must include, in an on-line supplement to their manuscript submission, a list of all articles (in AJO reference format in alphabetical/date order (by authors’ names and then publication year) that were identified from any information source. For each article, this list must include how the article was identified and whether the article was included (in the systematic review, in the meta-analysis, and in any subgroup analyses or, if not included, the specific reason(s), based on each applicable inclusion and exclusion criteria, why it was not included). Note that the reason for not including an article can be based on reading the title alone, as is appropriate for screening articles. (See Higgins JPT, Deeks JJ. Chapter 7: Selecting studies and collecting data. In: Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions. Chichester, UK: John Wiley & Sons Ltd; 2008:151–186.)

6. Data collection process:

a. Proposal (planned)

b. Manuscript (changes from proposal only)
7. Data items:
   a. Proposal (planned)
      1) AJO instructions: A copy of the planned data collection instruments (forms) must be provided.
   b. Manuscript (changes from proposal only)
      1) AJO instructions: A copy of the final data collection instruments (forms) must be provided. **This need not contain the data.**

8. Risk of bias of individual studies:
   a. Proposal (planned)
      1) AJO instructions: Include an assessment of confounding (e.g. comparability of (1) treatment & control groups in randomized control studies, (2) exposed & unexposed groups in cohort studies, (3) cases & controls in case-control studies, and (4) groups that are compared in any study, when appropriate)
   b. Manuscript (changes from proposal only)
      1) AJO instructions: Indicate relevant table(s) and/or figure(s).

9. Summary measure(s).
   a. Proposal (planned)
   b. Manuscript (changes from proposal only)

10. Synthesis of Results: Describe the statistical methods for combining the results of studies:
   a. Proposal (planned)
      1) AJO instructions: Note the requirements under “Description of statistical methods” in the table of the MOOSE document. Note, the proposed statistical methods for combining the results of studies must be appropriate for meta-analysis.
   b. Manuscript (changes from proposal only)

11. Risk of bias across studies
   a. Proposal (planned)
      1) AJO instructions: This should include quantitative assessment of biases.
b. Manuscript (changes from proposal only)

1) AJO instructions: Indicate relevant table(s) and/or figure(s).

12. Additional analyses:

a. Proposal (planned)

1) AJO instructions: Describe any anticipated subgroup analyses, sensitivity analyses, meta-regressions, etc.

b. Manuscript (changes from proposal only)

1) AJO instructions: Indicate relevant table(s) and/or figure(s) of results.

13. Assessment of the quality of each included study

a. Proposal (planned)

b. Manuscript (changes from proposal only)

1) AJO instructions: Indicate relevant table(s) and/or figure(s).


a. Proposal (planned)

b. Manuscript (changes from proposal only)

1) AJO instructions: Indicate relevant table(s) and/or figure(s).

E. RESULTS

1. Results of individual studies:

a. Manuscript

1) AJO instructions: Provide a table describing each included study. Although some tables may be on-line only, generally a table describing all articles in the meta-analysis would be included in the print meta-analysis article. A separate table (online) should be included if there are many articles included in the systematic review that are not included in the meta-analysis.

2. AJO instructions: In the results section, provide other appropriate tables and figures (see section D above). Some tables and figures may be on-line only. If applicable, provide an explanation of why a meta-analysis was infeasible.
F. DISCUSSION

1. Summary of evidence:
   a. **AJO instructions**: Describe how well the included studies address the clinical question. Interpret the results in the context of the existing medical literature.

2. Limitations:
   a. *In the proposal, describe any anticipated limitations.*
   b. **Manuscript (changes from proposal only)**

3. Future research:
   a. **Manuscript**

4. Conclusions:
   a. **Manuscript**

   1) From MOOSE document: Reporting of conclusions must include (when appropriate) alternative explanations for the results and appropriate generalization of the results within the overall context of the literature review. Describe how and why clinical practice will be affected by the results.

G. FUNDING:

1. Proposal (planned)

2. Manuscript (changes from proposal only)