Reviewer's report

Title: Prosthetic heart valves in pregnancy: A systematic review and meta-analysis protocol

Version: 1 Date: 15 October 2013

Reviewer: Susanne Hempel

Reviewer's report:

Very interesting topic. Here are my comments:

Major compulsory revisions
The PROSPERO number should be added to the abstract.

It is not clear how the reporting guideline MOOSE fits into the inclusion criterion for eligible Study types in the Eligibility criteria for consideration of inclusion section; the criterion should be clarified.

Generally, it would be useful to provide more detail to the eligible study designs in the inclusion criteria section. Currently it is not clear what the study characteristics are that make a study eligible for inclusion. The analysis plan suggests that studies will compare adverse events rates of women with prosthetic heart valve compared to other women but the inclusion criteria suggest that this will only be a subset of studies; most studies will be uncontrolled or use other comparators. The comparator should be specified further.

The subheadings "Inclusion criteria" and "Exclusion criteria" in the Eligibility criteria for consideration of inclusion section should be replaced with more specific headings - the entire section states inclusion and exclusion criteria (or should be added to existing subheadings with criteria relevant to participants added to “Participants” paragraph etc.).

I think the “at least six pregnancies” need to be explained in the method section – why six?

In addition, if there are six eligible participants does the greater than 5% of the study population with a Starr-Edwards valve still apply?

The data analysis plan is very specific and does not seem to match the large scope of eligible study designs. It is unlikely that all included studies will report adverse events rates for women with and for women without heart valve replacement. There should be an analysis plan for all included studies, in particular the uncontrolled studies and studies comparing different management regimens rather than women with or without heart valve replacement.

Differences in subgroups should be meta-analytically investigated not through t-tests.

The role of the funding agency should be described.

Minor essential revisions
The abstract should mention the process for inclusion screening. The duplicate approach is even more important for title and abstract and full text screening. The title and abstract screening is an essential part of a systematic review. I would suggest revising the sentence “Article titles (+/- abstracts) will be evaluated for potential relevance prior to formal review.”

Hand searching is not the same as reference mining; the sentence should be revised.

It would be better to describe the title and abstract screening and the full text screening separately. Presumably you will not reconcile title and abstract screening decisions but instead obtain all potentially relevant publications. The full text screening on the other hand will follow the explicit inclusion criteria will be reconciled and there is a mechanism in place to handle disagreements.

The descriptive characteristic item “mode of delivery” seems misplaced in the Secondary outcome section.

How will the quality of the randomized controlled trials be assessed (also an eligible study design)?

I suspect that most studies will not be suitable for a comparative adverse event meta-analysis therefore I would rephrase the sentence “Comprehensive Meta Analysis …will be used for the data analysis.”

It would be useful to outline the strength of evidence assessment in a separate paragraph.

Discretionary Revisions

The objectives are more general than the inclusion criteria (outcomes versus adverse events); it would be useful to align the sections.

I think heart valve prosthesis insertion could be called an intervention instead of “Exposure of interest”.

Clinical trials (non-randomized but group assignment by investigator) are presumably also eligible and should be added to the list.

Given the topic it would be useful to search CINAHL for relevant studies.

This protocol should probably include the preliminary search strategy for one database, e.g., exact search strings for MEDLINE.

I would suggest adding a mock up evidence table to this protocol. This will help to decide with characteristics are important for the presentation of study results. I would also suggest using some examples of studies to try out the evidence table.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests.