Reviewer's report

Title: Low-molecular-weight heparin for prevention of placenta-mediated pregnancy complications: protocol for a systematic review and individual patient data meta-analysis (AFFIRM)

Version: 3 Date: 9 April 2014

Reviewer: Andrew Booth

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1. The protocol is well structured and contains all the features one would expect from a meta-analysis of individual patient data. A particular feature is the strong consensual process with involvement from all relevant principal investigators.

2. The methods are transparent and clearly articulated. There is a clear relationship with a predecessor literature based review. There is a very clear itemisation of outcome measures.

3. As far as I can tell the statistical analysis is appropriate. However I am not a statistician. I would assume that the protocol, unlike a completed study, would have been extensively peer reviewed as part of the funding process where appropriateness of statistical techniques is rigorously scrutinised.

4. Generally the writing is of a very high standard and the protocol is clear to follow.

The following discretionary minor amendments are suggested:
“liberally” use “universally” as it more accurately indicates coverage rather than application.

Needs references for side effects – major and minor.

“lamentably, does not recognize them as an important patient group in which to develop clinical trials” – I think they probably “recognize” them but, for the preceding reasons, do not “acknowledge” them!

“Those RCTs that exist are all academically driven.” – needs to finish this sentence as to why this is a problem.

I believe it should be “an LMWH” not “a LMWH” but there is unfortunately not a consensus.

It is confusing that there are some protocol activities that have already been done and others that remain to be done. The problem is that the authors switch between the two. Either the events should be presented chronologically or the authors should write the protocol in methodological order with a note at the end that certain events e.g. meetings have taken place by the time of writing giving opportunity for exact dates. I think the main problem for this is the section on Methodological Quality Assessment which subsequently appears to have been completed so maybe it is simply about changing the tenses in this section?
“practising” not “practicing”

“knowledge users who are familiar with current clinical practice and practice environments” – all clinicians are knowledge users! This is unnecessary jargon so perhaps emphasise that this refers to this particular topic area.

In addition I would suggest the following as a compulsory amendment:

Tables 1, 2 and 3 – the order of trials should be either alphabetically by trial name (or by author) or chronologically. A haphazard presentation of trials makes reference and lookup more difficult.