Reviewer's report

Title: Unintended effects of statins from observational studies in general population: systematic review and meta-analysis

Version: 1 Date: 29 November 2013

Reviewer: Michael J Blaha

Reviewer's report:

1. Major Compulsory Revisions
   - None.
   - I find this to be a high quality manuscript with no obvious methodological concerns (at least ones that have not already been pointed out by the authors themselves).
   - I would like to congratulate the authors on this huge undertaking.

2. Minor Essential Revisions
   - There are a few spelling mistakes in the text, but nothing major that cannot be fixed during copyediting.

3. Discretionary Revisions
   - I think the abstract could be much better
   - In the background section, "safety" is used in the first sentence and "unintended effects" in the next sentence. These aren't necessarily the same thing. A drug may be unsafe through an intended effect (hypoglycemic for a hypoglycemic drug, etc). Safety is commonly reported in trial, however I agree that unintended effects are not commonly reported. Consider changing word "safety" in first sentence.
   - In the background, "from general populations" is much too vague. Consider removing this phrase all together.
   - In last sentence of background, use the RCT abbreviation you have defined.
   - In methods, "hospital based cohort studies" is not a clear description to me. Consider being more specific, or at least describing more in the body of the text.
   - In results, please give total number of patients studied with mean follow-up time, total years at risk, or some other measured of duration of follow-up available.
   - In results, recommend also giving effect sizes for the "positive" outcomes: myopathy, liver, diabetes.
   - In conclusion, first sentence appears to be a general methodological statement and doesn't even mention statins. Consider "We show that systematic review and meta-analyses of high quality observational data may can provide critical data on
unintended effects of statins missing from RCTs"

- In conclusion, the last sentence should specifically mentions statins as a class of drugs. Consider: "The absolute excess risk of harmful unintended effects of the statin class of drugs is very small compared to the beneficial effects on major cardiovascular events."

- please consider the following new citation:

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

No declarations.