Reviewer's report

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

Version: 1 Date: 6 February 2014

Reviewer: Yoon Kong Loke

Reviewer's report:

Major compulsory revisions

I have focused my comments mainly on the Methods:

The search is now two years out of date; last conducted January 2012.

If you used the BMJ Cohort studies filter, how well do you think it would have worked in picking up Case-Control studies?

The Discussion section should mention the important Limitation that Data Extraction and Validity Assessment were mainly carried out by a single reviewer (I appreciate that a random 10% of the extraction was checked).

Sensitivity analyses – the cut-offs for various subgroups seem somewhat arbitrary, I assume that these were categorized posthoc? Why use the threshold of 8 for NOS quality? The subgrouping according to sample size is somewhat meaningless when there are different study designs in this review. For instance, you could have a very large cohort study with very few events of interest, whereas you could have a much smaller case-control design that has hundreds of cases with outcomes of interest.

This review does not seem to consider outcome reporting or publication bias. Case-control studies may only have reported drug use or exposure where a significant association was found. Similarly cohort studies may only have provided numerical estimates of the association where significant findings were noted, and there may have been outcomes where the primary studies simply stated no significant harm was found. These data would not have been included in the present meta-analysis; hence I view it likely that the pooled effect sizes may potentially be exaggerated by this bias. I appreciate that this is hard to deal with or to address, but the major limitation should be acknowledged.

Results section:

I think you should present an Online Supplement with Forest Plots of each outcome showing effect estimates and 95% CI from the individual primary studies. This gives a better visual depiction of the heterogeneity amongst studies when considering the pooled value within the meta-analysis.

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