Reviewer's report

**Title:** Peginterferon alpha based therapy for chronic hepatitis B focusing on HBsAg clearance or seroconversion: a meta-analysis of controlled clinical trials

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**Reviewer:** James Guevara

**Reviewer's report:**

The manuscript entitled “Peginterferon alpha based therapy for chronic hepatitis B focusing on HBsAg clearance or seroconversion: a meta-analysis of controlled clinical trials” is a systematic review and meta-analysis of controlled trials evaluating pegylated interferon alpha for the treatment of chronic hepatitis B. The results of 14 eligible trials suggest that this therapy was more effective than lamivudine or conventional interferon alpha in HBsAg clearance and seroconversion. The authors should be commended for their hard work in conducting this important study. Enthusiasm for this study is muted by a number of issues that need to be addressed by the authors.

**Major Revisions**

1. The authors restricted eligibility to English- and Chinese-language publications. This raises concerns for publication/language bias, yet no tests for publication bias were conducted. The authors should assess for publication bias using standard procedures, e.g. funnel plots, Begg or Egger tests, and then comment on the degree to which their results may have been influenced by publication bias.

2. The authors stated that they assessed for heterogeneity using the Q-test and I² square test, yet there are no subanalyses examining for heterogeneity. An important aspect of meta-analysis is to explore for heterogeneity, which can be accomplished by preplanned stratified analyses or meta-regression analysis. The authors should consider an exploration of the effect of study quality and any other stratified analyses on their outcomes.

**Minor Revisions**

3. The background is too brief and does not provide the rationale for why the authors are comparing pegylated interferon alpha compared to conventional interferon alpha and/or lamivudine.

4. Details of the literature search are cursory and need additional details including years searched, which previous publications were manually searched, and whether there was contact with any experts in the field to identify additional papers. The concern is that the literature search may not have been extensive enough.

5. The main outcome used for the pooled estimates was an odds ratio. It’s not clear why the authors didn’t select a different outcome measure such as relative...
risk or risk difference. In addition, they likely encountered cells with “0” which would not permit the calculation of a summary OR. How did they deal with “0” cells?

6. In the results, the authors state that they excluded two trials that differ from the others but don’t explain further. Were these studies that otherwise met eligibility criteria for the study? If so, it’s not clear why they were excluded.

7. In the discussion section, the authors conclude that pegylated interferon alpha produced significantly higher HBsAg clearance and seroconversion. Although this is true, the absolute change in the proportion with HBsAg clearance and seroconversion was low (@ 3-6%). The authors should address this issue in their conclusions and discuss whether additional interventions are needed to enhance the low rate of positive outcomes.

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

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests