Reviewer's report

Title: Comparing influenza vaccine efficacy against matched and mismatched strains: A systematic review and meta-analysis

Version: 3 Date: 28 March 2013

Reviewer: Heath Kelly

Reviewer's report:

Comments on revised manuscript

The authors have made almost all the changes and clarifications that I requested. The change to Table 1 requested by Dr Beyer has been very useful. However I think a little work is now needed on the revised results. I assume that the initial aim of this study was to provide VE estimates for mismatched strains, as far as that is possible from the published literature. However most readers will be interested in the comparison of matched and mismatched VE estimates (in that order).

1. May I suggest that results for matched strains are presented before mismatched strains in the results? Matching is what strain selection committees hope to achieve after all.

2. The justifications for reporting only LAIV for 6-36 months and TIV for adults might need rethinking. In Australia only inactivated vaccines are licensed for all ages. The cut-off for LAIV in the funded program in the UK will be 16 years. Most RCTs of LAIV include children up to 7 years.

3. The paragraph between lines 238 and 241 does not appear to make sense. Matched and mismatched vaccines are both significantly protective. The second sentence begins, “In comparison...”

4. The next paragraph notes ‘drifted B strains’ and ‘lineage drift’. Presumably drift within lineage and lineage mismatch?

5. I2 is reported only for Figure 6 (line 255).

6. Dr Beyer found the results difficult to read and I can see his point. Too much information is contained in parentheses. An alternative way to present the results might be something like the following: VE against matched strains provided by TIV was 62% (95% CI 51-71) for all ages and 65% (95% CI 54-73) for adults. For mismatched strains ....

7. Why have you elected not to formally test differences in VE, preferring to say that VE is slightly different when the (usually quite wide) CIs overlap? I think this is bad habit into which many of us have fallen (myself included).

8. The first sentence of the discussion could now include matched and mismatched vaccines.

I appreciate the enormous amount of work that has gone into this paper and continue to believe it will be a useful addition to the influenza meta-analytical
literature. While the exposition of match is not perfect, it is far better than any published analysis of VE by match.

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

no competing interests