Reviewer's report

**Title:** Influenza vaccines licensed in the United States in healthy children: A systematic review and network meta-analysis (Protocol)

**Version:** 1  **Date:** 18 October 2012

**Reviewer:** Brian Hutton

**Reviewer's report:**

Overview:
In this protocol the authors describe their proposed methods for a systematic review with network meta-analysis of influenza vaccines. The proposal appears important and relatively well planned. Some general comments on the methods described are provided below for consideration for potential updates to the protocol manuscript.

General Comments:

- In paragraph 1 of the background, appears a comma should be used rather than a semi-colon after ‘worldwide each year’. In the second paragraph, appears the word ‘emphasizes’ should be the word ‘emphasis’.
- On the fourth line of the first paragraph under study objectives, is TIV a typo that should be IIV?
- The study objectives notes that one of the objectives is to identify optimal vaccines for each age group, yet in the analysis description this subgroup is mentioned very low down in the details. Suggest moving this further up if this is a key objective.
- Have the authors checked that their inclusion criteria are in line with the existing reviews they plan to make use of? If not, how will this be addressed with regard to study selection?
- The authors note they will use the lit searches of the existing reviews found and will re-run them to identify studies outside their current timeframe. Will the authors appraise the strength of the searches of the existing reviews to ensure they are not weak and possibly prone to missing studies?
- The authors mention making use of the newcastle ottawa scale for observational studies and having no scoring system. This is a limited, unvalidated scale and I wonder if the authors would be better suited to the Downs and Black scale. The protocol should also note what will be done with this assessment exercise in their work.
- The authors describe looking at I2 values, but do not actually note how they will be used to decide not to pool data. Is >50% being implied? This should be explicit if so. Also, what will be done if pooling is not appropriate?
- The authors note using Lumley’s approach for network meta-analysis. The
bayesian approach for network MA does not generate RRs without assuming rarity of the event and I am wondering if this is the case for Lumley’s approach also. Do the authors need to specify any assumptions here?

- The bayesian approach allows intuitive estimation of treatment rankings and probabilities of superiority that can be helpful for interpretations. Have the authors considered using this approach for these reasons?

- An important assumption for network MA is homogeneity/similarity. The authors should note how they will assess these for the included data.

- For Reporting, the authors should consider following ISPOR/NICE guidance on how to best report findings from a network meta-analysis and mentioning this in the protocol.

- The authors comment in the discussion that existing reviews ‘appear quite comprehensive’. How was this determined? By AMSTAR? This should be done/clarified.

- In addition to the table for the GRADE profile, the authors could include a table outlining the data they’ll capture in evidence tables to describe the studies and verify homogeneity/similarity.