Reviewer’s report

Title: A systematic review on the effect of sweeteners on glycemic response and clinically relevant outcomes

Version: 1 Date: 6 July 2011

Reviewer: Sofia Dias

Reviewer’s report:

Discretionary Revisions

1. Authors are invited to consider adding rank-o-grams (plots of the probabilities that each intervention is the best, 2nd best etc) to show efficacy of the various interventions considered in the network meta-analysis on the multiple outcomes. For example of rank-o-grams see:
   Cipriani et al. (2009) Comparative efficacy and acceptability of 12 new generation antidepressants: a multiple-treatments meta-analysis. Lancet 373, 746-758 and

Minor Essential Revisions

2. Present the confidence intervals for the numbers quoted in the Abstract, or clarify if already doing so.

3. The choice of an active control group should be explained in the Introduction.

4. It should also be clarified that cross-over trials are not appropriate for weight-loss outcomes and are not included. Also, a (short) justification of why cross-over trials are suitable for the other outcomes would be reassuring.

5. Page 9, reference 19 for network meta-analysis: although Salanti et al provide a good review of methods, the appropriate reference to network meta-analysis is “Lu, G and Ades, AE. Combination of direct and indirect evidence in mixed treatment comparisons. Statistics in Medicine 23, 3105-3124. 2004” and this should be changed.

6. Page 9, sentence “Network analysis extends meta-analysis from simply pooling directly compared treatments (direct evidence) to pooling data from studies not directly compared but linked via one or more common comparators (indirect evidence)”: add “… by assuming consistency of the evidence” or similar and cite Lu & Ades, Stat Med 2004.

7. Page 9: State what was the range of the uniform prior and what were the mean and variance of the Gaussian priors.
8. State which STATA command was used to perform the pairwise meta-analysis and where the WinBUGS code was obtained from. If new code was written then this should be provided for review and published in an Appendix. Also state how convergence of the MCMC algorithm was assessed, how many burn-in iterations were used and how many samples were taken from the posterior distributions after convergence.

9. Page 12: The data in Tables 3 and 4 have different network structures and this needs to be made clear.

10. Page 12 “2-hour blood insulin response”: the authors state that incoherence was detected – was this investigated further? If not, then there is no point in looking for incoherence if noting will be done about it! There are several statements throughout the manuscript stating that incoherence and high heterogeneity were present, but no attempt is made to explain them.

11. Page 14, 3rd paragraph: Are cross-over trials appropriate for weight-loss outcomes? Please justify (also see comments about introduction above).

12. Page 16, 3rd paragraph: “Seven trials reported change in total cholesterol...” Justify why no network meta-analysis was done on the treatments compared in these trials.

Major Compulsory Revisions

13. State the value of the estimated heterogeneity (and confidence intervals) throughout the results for all pairwise and network meta-analyses. Furthermore, a statement of whether the WinBUGS.

14. In the Discussion, the authors must comment on the draw-backs of the back-calculation method used to assess incoherence. In particular, the fact that when random effects models are used for the separate MA inputs, different heterogeneity parameters are being estimated. The results are therefore hard to interpret if heterogeneity is very different between the different pairwise MA and the NMA. The node-split method recommended in Dias et al [20] is better in these circumstances, as is the new (and simpler) method for assessing inconsistency described in Dias et al 2011 TSD 4 – available from http://www.nicedsu.org.uk/Evidence-Synthesis-TSD-series%282391675%29.htm

The impact of the different heterogeneity estimates will of course depend on their values (which should be presented as mentioned above) and this needs to be discussed and justified.

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