Reviewer's report

Title: Dietary iron intake, body iron stores, and the risk of type 2 diabetes: a meta-analysis

Version: 1  Date: 28 June 2012

Reviewer: Darren C Greenwood

Reviewer's report:

Major compulsory revisions:
1. Unfortunately, comparing the highest category of exposure with the lowest for each study, fails to quantify the association fully. Different studies use different categorisations, introducing heterogeneity, and meaning that the definition of “highest category” is different for each study. This in turn makes it impossible to interpret the results, because we do not know what exposure the increased risk relates to. In addition, it ignores most of the data, so that the results are based on far far fewer than the 9,269 incident T2DM cases from 197,488 participants quoted. Instead, the authors should model a dose-response trend over the intakes using methods such as that of Greenland and Longnecker, otherwise results are uninterpretable.

2. Heterogeneity. There is heterogeneity, and the authors completely fail to address this. There should be a detailed analysis of potential sources of heterogeneity – this could explain some of the differences in results between the studies. Maybe there are too few studies to do this properly, but this is a weakness in the interpretation of the results.

3. The abstract does not give the non-heme iron, supplemental iron and total iron intake results. The pooled RRs and confidence intervals for all meta-analyses must be included to give a balanced summary. The conclusion to the discussion also ignores all the non-significant results. Again, these should be given equal weight in the conclusions.

Minor compulsory revisions:
1. The authors used hand-searching, but have not included this in their flowchart. This is important as a measure of how good the original search strategy was.

2. Page 5. The model with the largest number of covariates is not necessarily the most appropriate, and may lead to over-adjustment.

3. Page 6. HR are already RR, and need no rare disease assumption. You only need the rare disease assumption for OR. The authors argue that they can combine HR and OR with RR as they are all estimates of RR. However, that does not mean that the authors can refer to OR as RR, because they are not. Report OR as OR, but combine with HR and RR in the forest plots.

4. Page 6. Funnel plots do not assess publication bias; they assess small study effects. One of which is publication bias. But in nutrition epidemiology the smaller
studies may well have better methods of assessing the exposure, so it could be that the larger studies are the ones with greatest bias.

5. The numbers of studies in the meta-analyses are too small for adequate assessment of small-study effects.

6. Page 3, paragraph 2, line 2. “in human” should be “in humans”.

7. Page 4, final line. “for EMBASE database” should either be “for the EMBASE database” or “for EMBASE”.

8. Page 7, last paragraph, penultimate line. “one studies” should be “one study”.

9. Page 8, first paragraph, last line. “noon-heme” should be “non-heme”.

10. There is no need to quote I squared values to one decimal place, nor p-values to 3 decimal places. This creates a false sense of precision in these figures.

11. To avoid reverse causality, the authors need to do more than just exclude retrospective studies, they should also consider exploring exclusion of studies with diabetes incident within, say, 2 years of iron intake being recorded.

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.