Reviewer's report

**Title:** Dietary Calcium Intake and Risk of Mortality from Cardiovascular Disease and All Causes: A Meta-Analysis of Prospective Cohort Studies

**Version:** 1  
**Date:** 15 May 2014

**Reviewer:** Darren C Greenwood

**Reviewer's report:**

General comments to authors:
A well written paper investigating dietary calcium intake in relation to risk of CVD and all-cause mortality.

Major Compulsory Revisions:
1. Figure 2 is a lovely graph, but there are a number of things that appear very wrong with it. The authors state that the reference intake is 800g/day, so the relative risk at 800g/day should be 1, because everything is relative to that intake. But *all* relative risks are above 1. That cannot be correct. Furthermore, at the reference intake, the standard errors should be zero, because the relative risk is fixed as 1.0. But the confidence intervals on the graph do not reflect this. I can only conclude that there is something wrong with either the plotting of the graph, or worse the model on which it is based. The graph for all-cause mortality in the supplement seems have done this better, so it is worrying that CVD mortality does not. The authors need to look into this.

2. Results for men and women from the same study are included in the meta-analysis as if they were from separate studies. This leads to under-estimation of the heterogeneity and wrong tests of heterogeneity. Instead, the authors should first combined the results from the men and the women separately using fixed effects, so that each study only has one result, before combining with the other studies as normal.

3. There is some inconsistency in the reporting of heterogeneity. Some meta-analyses have it, some don’t. But more importantly, there is no exploration of this heterogeneity. There should be, and this would form a useful addition to the review.

4. A final comment is that investigating CVD mortality a quite different thing from CVD incidence. The introduction and aims suggest that such CVD events are what the authors are really interested in, but have not looked at. Hypothetically you could have different causes.

Minor essential revisions:
1. The axes on the forest plots would benefit from better labelling and numbers on the axes.

2. Both CVD mortality and all-cause mortality should ideally use the same
reference intake so that we can compare the curves.

3. It would be helpful to see the levels of intake contributing to the curves indicated on the graph, so the reader can see where the bulk of the data is, and how many studies / observations are in the extremes.

4. The authors state “A test for a nonlinear relationship was calculated by setting the coefficient of the second spline equal to zero.” Constraining the coefficient to be zero is not of itself a test. Maybe they then compared this to an unconstrained model? Maybe they simply tested the null hypothesis that this coefficient was zero? This should be put more clearly.

5. It is not clear whether the dietary calcium intake used as the main exposure includes dietary supplements or not. Isn’t total intake the most relevant exposure? Maybe the authors could be clearer on this in the methods and descriptive tables.

6. Calcium absorption may be modified by vitamin D status. Several of the included studies report on this. This would therefore be an important subgroup analysis to explore this potential source of heterogeneity in the results. In the absence of adequate information on vitamin D status, would latitude be a useful proxy?

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I have received grant funding from Danone plc for two small projects unrelated to this work. I declare that I have no other potential competing interests.