Reviewer's report

Title: Spousal diabetes as a diabetes risk factor: A systematic review and meta-analysis

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Reviewer: Ross Harris

Reviewer's report:

This study presents a systematic review of spousal diabetes as a risk factor. It makes for interesting reading, and the authors have conducted the study carefully. The conclusions are well-thought out and interesting, although I have some concerns that some of the final conclusions have little evidence basis. In general though, this is a very interesting paper and for the most part needs only minor improvements.

Major Compulsory Revision:

In the discussion, the authors mention that the true effect is likely to be higher than their pooled estimate, and more akin to the highest estimate of all studies. I think this is a dangerous conclusion: why is this study likely to be the most representative? The only cohort study available, which is well-recognised as being a preferable study design, could as well be taken as the “best estimate”. This study did not adjust for BMI, but given that adjusting for BMI would be more likely to attenuate effect estimates, the more modest association in Hemminki makes me wonder whether the effect is really as strong as the authors speculate. Further, the authors are, in a way, discounting the results of their own meta-analysis – if they felt that the studies were not comparable, they should not have combined them in a pooled estimate. The study by Khan is given the highest quality score, but this is based on a somewhat subjective method, which the authors have further modified. The confidence interval for the study by Khan is also very wide, indicating substantial uncertainty in their results. I therefore struggle to see the reasoning behind this. The authors state that this may be due to the “systematic glucose testing” employed by the study – if this is the case, then further explanation of how not using this method would weaken the association should be presented. The authors state “It may be easier to capture concordance for diabetes/prediabetes than for diabetes alone because diabetes/prediabetes has a higher prevalence” – but odds ratios or other measures of association should not depend on background prevalence, so the reasoning here does not make sense to me. In any case, the authors should keep in mind the wide confidence intervals of the Kahn study, and the conclusions should be more cautious.

Minor Essential Revisions:

There is not much evidence to go on here: although a pooled estimate may of course be derived, performing subgroup analyses is going to be somewhat akin
to randomly selecting subsets of studies. The authors should be careful to acknowledge the limitations in comparing small subsets of studies, or even the results of single studies, and the danger of chance findings (see, e.g., Higgins et al, Controlling the risk of spurious findings from meta regression, Statsmed 2004) – the authors acknowledge that there are too few studies for meta-regression, which also precludes any other valid subgroup comparisons, and therefore need to be cautious in their conclusions about different ethnic groups, etc. Further, the authors should acknowledge the small number of studies, and heterogeneity in their results, in the strengths and limitations section. With the evidence available there is no possibility for exploring differences between studies.

Abstract – not clear what the “effect” is – if a mix of OR/IRR could just say “relative risks”

P12, meta-analysis “There was suggestion of heterogeneity (Higgin’s I-squared statistic = 65.4%, P-value = 0.03)” – I would say “some evidence” of heterogeneity, given the low p-value.

Table 1: marriage duration in Kim 2006 says “530” – not clear what measure this is, or what the “(16.9)” is (standard deviation?). Also, the second half of the table appears to be pre-diabetes, but this is not clear.

Discretionary Revisions:

The Newcastle-Ottowa scale has been used to evaluate risk of bias. Although this provides an easy-to-use measure of study quality, its limitations should be considered by the authors: in general, Cochrane guidelines do not recommend the use of summary scores, particularly for analytical purposes, and generally prefer the use of checklists and so on. It must also be borne in mind that the reference for the NOS is not from a peer-reviewed publication, and aspects of it have been criticised (see, e.g., Stang A, European Journal of Epidemiology 2010). However, the authors have given good descriptions of the individual studies and their limitations; therefore I have no particular criticism apart from whether it has led to the specific part of the conclusion that I am concerned about above.

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