Reviewer's report

Title: Increased Risk of Depression in Type 2 Diabetes Is Minimised by Sulfonylurea and Metformin Combination: A Population-Based Cohort Study

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Reviewer: Frans Pouwer

Reviewer's report:

Wahlqvist et al have written an interesting study on incident depression in diabetes, using a huge, impressive dataset.

1. Is the question posed by the authors new and well defined?

Not completely new: the question whether diabetes is associated with a higher incidence of depression has been the subject of a systematic review of Nouwen et al, Diabetologia, 2011. This systematic review with meta-analysis should be included in the introduction. Nouwen et al Diabetes Care 2012 have also conducted a systematic review studying whether pre-diabetes/undiagnosed diabetes/diagnosed diabetes are associated with depression. Both reviews are currently omitted and should be included. The association between oral medication use and incident depression is new. Another recent study that is relevant for the introduction, that I am aware of is Nefs et al, Diabetologia, 2012 (course of depression in DM2)

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?

No. I believe there are several important methodological shortcomings:

2a) If one aims to study incident depression in a certain sample, depressed cases should be excluded at baseline. Wahlqvist et al did not do this. I cannot find this in their description of study 1 page 6/7.

2b) The authors aim to study the effects of oral anti-hyperglycemic agents (OAA) on incident depression. No information is given about another important factor that is closely related to OAA: insulin therapy (yes/no). People with type 2 diabetes who use insulin often have the idea that they have a more severe form of diabetes + the have a more intensive treatment regimen + more fluctuating blood glucose levels

2c) Figure 1 is unclear. How many patients without OAAs used insulin? Depressed patients should be excluded at baseline

2d) Page 7: it is stated that the authors compared incidence of depression in DM-free, DM on OAA end DM without OAA. Why did the authors not compare SUD's versus metformin versus both?

2e) It is very unclear how depression was measured, the most important variable
of the study. Physician detected depression? There is a considerable under-detection of depression in diabetes.

2f) Do the authors have data about type of diabetes? How did they determine DM2?

3. Are the data sound and well controlled?
   yes

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   yes

5. Are the discussion and conclusions well balanced and adequately supported by the data?
   I have so many questions regarding the analyses, that I did not read the discussion.

6. Do the title and abstract accurately convey what has been found?
   No, regarding the abstract: it is unclear 1) whether depressed patients were excluded from the baseline 2) whether the group without OAA’s included patients on insulin.

7. Is the writing acceptable?
   yes

   **Quality of written English:** Acceptable

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

   **Declaration of competing interests:**

   I have no competing interests