

Dear Editor,

**Manuscript ID BMJ.2015.027737.R1 entitled "Antidepressant use and risk of cardiovascular outcomes in people aged 20 to 64: cohort study using a primary care database"**

Thank you very much for provisionally offering acceptance of this paper, subject to revision. We have revised the paper to address the issues raised by the BMJ in-house editorial review and have given our responses to each comment below.

Decision: Provisional acceptance

Detailed comments: We appreciate the thorough revisions and responses provided by your team to recommendations made by reviewers and editors. We have a few additional comments and look forward to your response to these:

\*There are some aspects mentioned in the response letter which we think might be helpful to include in the main paper as well for clarity:

1. The point in response to the standard comparison group that 'The comparison is then between rates of the outcomes in exposed and unexposed periods of time throughout follow-up.'

Response: We have added a sentence explaining this point to the Statistical Analysis section (page 9).

2. Inclusion of patients with a first recorded diagnosis of depression and that must have occurred at least 12 months after registration.

We have added the following text to the Study Cohort section (pages 6-7):

"We restricted our cohort to patients with a first recorded diagnosis of depression so that antidepressant prescribing during follow-up would not be influenced by previous experiences and preferences which would be difficult to account for in the analyses. The 12 month inclusion criterion was used to ensure that the diagnosis of depression was not a retrospective recording of a prior diagnosis. "

3. Rationale for the 5 year duration of follow-up

We have added the following text to the Statistical Analysis section to justify our rationale for the 5 year duration of follow-up (page 9):

"We selected five years of follow-up for our main analyses as this would incorporate periods of long term treatment, and also allow for more events to accrue than a shorter follow-up period so adding to the power of the study."

4. Why "year of diagnosis" is considered a risk factor

Response: We have added a sentence on this to the Confounding Variables section (page 8).

"We included year of diagnosis of depression as a confounding variable to account for changes in prescribing patterns over time."

\*We realize that a lot of the methodology and description of the cohort is similar to your earlier paper in The BMJ. It is also likely that the structure and organisation of the paper would be similar. However, we would like you to carefully cite the other paper in places where there is a lot of similarity.

We have now cited this earlier paper (reference 22) in several other places in this paper where there is a lot of similarity in the methodology and particularly where there is more detail in the earlier paper.