Reviewer's report

Title: Higher Anti-Depressant Dose and Major Adverse Outcomes in Moderate Chronic Kidney Disease: A Retrospective Population-Based Study

Version: 2 Date: 8 March 2014

Reviewer: Mariacristina Vecchio

Reviewer's report:

This is a retrospective cohort study of 117,811 old people (1609 with kidney disease) exploring the association between exposure to different doses of anti-depressant and the outcomes of hospitalization with urgent neuroimaging and 30 days all cause mortality.

Major Compulsory Revisions

1. The study takes good care of potential selection bias. People included in the cohort originate from the same general population and all older adults in Ontario exposed to higher or lower use of the three study antidepressant, are included. In order to stress this point authors may provide a more exhaustive overview of the source cohort before, during and after selection. Number of individuals at each stage of the study (potentially eligible, examined for eligibility (and reasons for non-inclusion), included in the study, analysed) may be reported in the text.

2. The methods used to identify the patient sample are clearly described and key characteristics of included population are well reported in table 2. The authors may consider to better describe this table in the text, adding a deeper explanation of the differences between the two groups.

3. The study also takes good care of potential confounding issues, by using a complex multiple level regression analysis which accounts for 15 confounders. Adjustment for mental disorders other than depression may also be interesting to explore.

4. Of 117,811 people included in the study, only a subpopulation of 1609 has CKD (number not reported in the text). If the study aims to analyze “higher anti-depressant dose and major adverse outcomes in moderate chronic kidney disease”, then authors may specifically study this target population (people with CKD).

Analyses may be run considering only the 1609 people with CKD as study population.

I also provide a list of point to point edits – comments to the various sections:

Abstract (Pag 2):

5. From here, it remains unclear the main objective of the study. Please state
specific aim/s.

6. Conclusions are general for people with CKD. Please specify that study population include old (mean 75y) people with moderate CKD.

7. The primary outcome of the study is here reported to be delirium defined as hospitalization with evidence of urgent CT scan. CT scan is used to investigate many central nervous system diseases, not only delirium. I don’t think we should assume that all patients undergoing a CT scan have delirium. Please, reword the outcome.

Introduction (Pag 3):

8. This background should be substantially improved. The paper is about the use of anti-depressants and the risk of major adverse outcomes in old people suffering CKD. Then the background should be reported as follows:

1. Prevalence of outcomes in the target population
2. Why is it a problem
3. Role of antidepressants as a potential effect modifier
4. What could be the mechanism?
5. Why are you doing this study? What are the open questions?

Discussion (Pag 12):

9. Missing info on cause of death is a great limitation of the study. It influences the results and their interpretation; it should be reported in this session
10. A session discussing the comparison with other studies may be added

Discretionary Revisions

Statistical analysis (Pag 7):

1. Specify how baseline variables are reported (meas (SD) for continuous variables/frequencies (%) for categorical variables)

Table 2:

2. Add “n(%)” to Modified Charlson score
3. Data on clinical history of study population should be reported with focus on mental disorders

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests