Reviewer’s report

Title: DEVELOPMENT OF A MORTALITY SCORE TO ASSESS RISK OF ADVERSE DRUG REACTIONS AMONG HOSPITALIZED PATIENTS WITH MODERATE TO SEVERE CHRONIC KIDNEY DISEASE

Version: 0 Date: 23 Apr 2019

Reviewer: Elisabetta Poluzzi

Reviewer's report:

The manuscript by Danial et al. deals with the risk of fatal adverse drug reactions (ADRs) in patients with chronic kidney disease (CKD). Authors aimed to develop a risk score to support clinicians in preventing death due to ADRs in this population, by performing a retrospective analysis on a sample of patients admitted to a large hospital in Malaysia. Specific variables impacting on death were identified by different models and appropriate scores were assigned to each of variables. Even the best developed model resulted in a modest performance, nevertheless the Authors stated that it can be clinically useful.

The topic of this study is certainly important by a clinical point of view and the Authors planned a number of methodological steps towards a definition of a performant model. However, many limitations should be considered.

1. I understand that the score aims to predict the risk of death of CKD patients experienced ADRs (not the overall risk of death in CKD patients, nor the overall risk of ADR with fatal outcome). The first aspect that should be clarified is in fact the exact aim and the coherent methodological approach. Authors seem to select patients with ADRs during hospitalization and to assess the risk of death in this specific subpopulation. If this is the case, Authors should make it clearer along the manuscript.

2. The overall risk of in-hospital serious ADRs in patients with CKD would also be a very important aim and it could be addressed with a larger eligible population and a relevant higher power of the analysis. As a matter of fact, only 160 patients were eligible for the present analysis and only 28 did not survive after ADR. The power of the study is very low and the modest performance of the model is probably due to this limitation. The causal relationship between ADRs and death in this population at high risk of death is very difficult to be established, because of the high number of risk factors (CKD and concomitant diseases).

3. The type of identified ADRs in eligible patients should be described, in terms of diagnosis and reported drugs, in a Table to be included in the main text.
4. The routine ADR reporting process in Malaysia should be better described (lines 85-90), also in terms of annual reporting rate (in-hospital vs. out-of-hospital), as well as in terms of percentage of serious ADRs.

5. The paragraph 132-136 should be moved to the results.

6. The discussion needs an extensive revision, by mainly focusing on ADRs and the relevant possible mechanisms rather than on concomitant diseases.

7. English language has to be strongly revised.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal