Reviewer’s report

Title: Epidemiology and health outcomes associated with hyperkalemia in a primary care setting in England

Version: 0 Date: 31 May 2018

Reviewer: Manish Tiwari

Reviewer's report:

This is a very well-written manuscript. It addresses a very important question in the field. Not much data is available regarding hyperkalemia and its effects. The question is very well researched. In addition, the manuscript is extremely well-written.

I have specific concerns regarding the study design and some of the results. Specific questions and suggestions for the authors are below. In its current state, the decision is REJECT.

1. Study design: I am not sure about the study design. It appears that the authors are performing a retrospective database analysis to answer this important question. In Methods section on page 5, they mention both a "cohort and case-control analyses." I am unsure if you can say both study designs have been used. It does not appear that this is a cohort study since the authors did not follow the patient population over 4 years. It maybe a case-control analysis. I would recommend that the authors or editor seek additional input from an epidemiologist regarding the study design.

2. Study statistic: The authors mention incidence and incidence rate throughout the manuscript. I do not believe that the authors can say this is the exact incidence of Hyperkalemia in the general population. I am unsure if the authors can report an incidence rate from database analysis. This again goes back to the point of recommending an epidemiologist to suggest the study statistic.

3. "Initial HK Event:" how can the authors be sure that the hyperkalemia event that they noted in a database analysis is the first event of hyperkalemia? It is very likely that the patients have had a Hyperkalemia event in past but that has not been captured because this is a database analysis during a certain time frame.

4. Age and first hyperkalemia event: In Table 3, the authors report unadjusted and adjusted OR for age and first hyperkalemia event. It shows age to be positively associated with initial hyperkalemia event in unadjusted OR. However, with adjusted OR, increased age shows less likelihood for hyperkalemia. the authors mention this in discussion but no discussion about why they think this is happening. Is this confounding, effect modification by a different variable or something else? I think what the authors are seeing is Simpson's Paradox although I cannot be sure given the details. Hence, I recommend the authors get suggestions from Epidemiology/Statistics to explain the effect.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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

Unable to assess

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

Unable to assess

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:

Acceptable

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