Reviewer’s report

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

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Reviewer: Manasi Bapat

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This is a large U.K. population-based study of the incidence and recurrence of hyperkalemia along with several important outcomes such as all cause mortality, hospitalization, acute and chronic decline in kidney function, RAASI use, need for dialysis, etc. The authors attempt to dive deep specifically into the recurrence rate of hyperkalemia after the incident event, medication use (RAASi/MRA etc.) associated adverse outcomes mainly cardiac (arrhythmias and cardiac arrest), AKI, dialysis, CKD progression and follow up testing or prescribed treatment.

Strengths-

1. Large database, adequately long follow up and large sample size

2. First large population-based study to ever report incident hyperkalemia events, patterns of retesting, outcomes and health care utilization.

3. The detailed analysis of outcomes following incident hyperkalemia event- cardiac outcomes, AKI/Dialysis etc. is a major strength of this paper.

Weaknesses/limitations/questions-

1. Title of the article is too long and needs to be succinct. E.g.- "Epidemiology and health outcomes of hyperkalemia: A population-based study"

2. Data obtained from ICD 10 codes is essentially administrative data hence possibility of many inappropriate/mis-classified diagnoses.

3. There is no mention of a major limitation here i.e.- possibility of inaccurately elevated levels of potassium which we often see due to hemolysis- this would not be reflected in the hyperkalemia diagnosis but will definitely impact lab-based detection, treatment, retesting and recurrence data.

4. Authors acknowledge the fact that majority of hyperkalemia cases were very mild so indeed may not require retesting. Those coded as severe hyperkalemia do have lower retesting rates but could be a result of several factors as above (initial inaccurately elevated levels due to
hemolysis, mis-diagnosis, subsequent lab tests done in ER instead of primary care etc.)

5. Only primary care visits are included in this study which is the source of the CPRD/HES database, ER visits are not accounted for which is likely the cause of low retesting rate found in this study. There also needs to be a clearer explanation and clarification as to how hyperkalemia was defined based on the three criteria- READ diagnosis, lab result and ICD 10 codes. The explanation provided in the "Patient Population" paragraph is not entirely clear. What if there was a hyperkalemia ICD diagnosis code in the patient's chart but no lab result? Were those patients still included in the study?

6. Data obtained from administrative codes also might have to do something with the surprising result that 57.7% of patients with severe hyperkalemia - K > 6 never used RAAS inhibitors! This seems novel in my opinion. Further exploration or comparison with other studies would be of interest to the reader.

7. Several results reported in this study are confirmatory - e.g.- association of ACEi with hyperkalemia, more number of co-morbid conditions with the group with severe hyperkalemia and the fact that baseline GFR was lower in the group with severe hyperkalemia.

**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.

Yes

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