Reviewer’s report

Title: Association of diabetic kidney disease with cardiovascular and non-cardiovascular outcomes: A retrospective cohort study

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Reviewer: Xiong-Fei Pan

Reviewer's report:

The manuscript examines the associations of diabetic kidney disease (DKD) with cardiovascular and non-cardiovascular outcomes using a commercial database that including 2.2 million patients with diabetes. It found elevated risks of both cardiovascular and non-cardiovascular outcomes among patients with DKD and those with only diabetes. The study is well designed with adequate statistical analyses and appropriate interpretation. There are, however, a few issues to address before it is publishable.

1. It is expected to have more detail about the study population (Page 5). The scope of the commercial database is not clearly defined. Why were only 2010-2014 datasets selected? It would be beneficial if earlier data were used with a longer follow-up.

2. The exposure of interest, DKD was defined as chronic kidney disease in diabetes patients (Page 6). The authors might need to acknowledge this limitation. It is possible that chronic kidney disease occurs before diabetes in certain patients, while after diabetes in other patients.

3. The follow-up was short in this study (Page 6). It is highly possible that certain outcomes occur before the DKD. Reverse causality cannot be ruled out. The authors need to discuss this.

4. Table 1: the sum of percentages was over 100% in certain columns. The authors might need to check the data and add footnotes below the table.

5. Table 2 and 3: It might not be helpful to list effect sizes for covariates if the authors were only interested in DKD. Particularly in Table 3, it is advisable to delete results for covariates. The authors may need to add footnote for the covariates and their variable types in the regression models. For example, was age treated as a continuous variable? The authors also need to acknowledge they only adjusted certain potential confounders available from the datasets. Confounders such as smoking and BMI were missing. It is
not clear why patients with CHF were included for analyses regarding outcome of CHF. There are similar problems with stroke and other outcomes.

6. Figure 1 repeats results in Table 3. The authors should only keep one of them.

7. Figure 1 and 2: The authors need to briefly introduce the main findings.

8. The authors might need to consider subgroup analyses by sex, age and other major covariates that may potentially modify the effect of DKD. This is more helpfully than listing results for covariates in Table 3.

9. While the present study design does not permit us to make inferences about the relative importance of kidney disease in patients with diabetes compared with patients without diabetes, it does permit estimation of the extent of the association between DKD and risk of major cardiovascular and non-cardiovascular outcomes. While other studies have attempted to estimate costs associated with DKD and its progression,16-19 none, to our knowledge, have explicitly quantified risk of morbid events (Paragraph 2/ Page 11). These two sentences are not logically reasonable.

10. The logical flow of the discussion section can be improved, and the authors need to compare to results from other cohorts in the US and other countries.

**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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