Reviewer's report

Title: Comparison of the Prevalence of Diminished Kidney Function and National Kidney Foundation Diagnosed Chronic Kidney Disease using the Different Estimating equations in a representative sample of the non-institutionalised Irish Population

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Reviewer: Austin Stack

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Author: Browne et al,

Summary

This is an important study as it is the first to describe the prevalence of CKD in a representative sample of the Irish population and provides useful insight into distributions across age and gender subgroups. The weighted prevalence estimates of CKD (GFR< 60 ml/min/1.73 m) are broadly similar in magnitude to other population-based studies in the literature, although there are some notable differences. A veritable strength of the study is the recording of albuminuria in the study sample which seeks to identify individuals with early CKD and provide more reliable estimates for overall prevalence. The study also draws attention to the now well recognised limitations of the commonly used MDRD equation by comparisons with the newly developed CKD-EPI formula. In addition, the authors provide insight on socioeconomic correlates of CKD, which while interesting are not particularly novel.

The study has some residual limitations, which this reviewer would like to see further addressed in a more comprehensive manner. These in general relate to 1) the focus on unweighted data rather than weighted estimations in the primary analysis 2) the general interpretation of the estimates and their validity in the context of selection bias arising from the sampling strategy and non-response rates, 3) systematic error arising from single estimations of albuminuria, and 4) a greater discourse on the potential limitations of this study. The authors might also consider providing the context for considering indicators of socioeconomic status and educational attainment. This should be discussed in the introduction section and would set the scene for their use in the subsequent analyses.

In general this population-based study adds to the existing body of literature on CKD burden from an Irish perspective while at the same time highlighting the deficiencies’ of MDRD based GFR equation for clinical use. While there are
some limitations and areas that require further clarification and fine tuning, I believe that all of these can be addressed by the authors

Limitations & Threats to Internal and External Validity

Major Compulsory Revisions

1. The external validity to all Irish subjects is limited by the fact that the original selected population in the SLAN excluded individuals < 45 yrs. This will of course eliminate younger individuals (a large proportion of which will have relatively preserved kidney function) and reduce the size of the denominator thereby increasing overall prevalence. Accordingly the estimates presented in this study really relate to middle to older age subjects in the Irish Population (rather than all adults) and any inferences on disease prevalence should explicitly acknowledge this both in the introductory abstract and its conclusion as well as throughout the text. Similarly, any comparisons of CKD prevalence with other national studies should specifically highlight the source population and age distribution to facilitate meaningful comparisons.

2. The authors present the unweighted estimates of CKD prevalence and stage of CKD in the primary analysis. Given that the study is based on a multi-stage sampling technique with differential probability of selection and with sizeable non-response rates and missing data, I feel that the primary data presented should be weighted data as a consequence of the study design. This will also permit more accurate comparisons with other international studies that have used this approach to estimate CKD prevalence in populations.

3. Both the unweighted and weighted prevalence estimates of CKD defined as GFR < 60 ml/min were generally higher than estimates generated from other population-based studies. For example the weighted CKD prevalence estimates of 14.86 % from MDRD (or 11.96 % from CKD EPI) were far higher than the 8.0 % from the NHANES 1999-2004. Indeed accounting for non-response and missingness, the weighted prevalence of CKD< 60 using CKD EPI was 11.8%, still appreciably higher than the weighted NHANES estimate of 8.0%. Although these differences may be attributed to other population characteristics (e.g. race, obesity, diabetes etc…), one might have expected a much lower prevalence in the non-institutionised Irish population. The higher than expected prevalence likely reflects the older sampled population and exclusion of subjects < 45 yrs. Additional commentary from the authors on this issue would be appreciated.

4. The inclusion urine specimens for albuminuria in the study is a veritable strength, although again, the reported prevalence of albuminuria, 13.2% is far greater than the estimates of 8.2% that reported in US and 6.7% in Australia. The magnitude of differences among studies is particularly noticeable when one looks at subjects with mild kidney impairment. The prevalence of albuminuria> 30mg/g was 13.8 % and 11.0 % in the > 90 and 60-89 ml/min categories respectively. This is substantially higher than the 7.9% and 8.2 % in NHANES 199-2004 subjects. The reasons for these discrepancies may well be due to differences in population characteristics across countries. However, it is more likely that the
age of the sampled population and the relatively small sample size within categories (wide confidence intervals) has limited the precision of the estimates. Finally, the current study based the presence or absence of albuminuria, which may be transient finding in some subjects and could easily have over-estimated prevalence (as compared with NHANES where 2 samples 2 weeks apart were required to confirm persistent proteinuria). This should be discussed by the authors and explanations offered for these differences.

5. Combination of Albuminuria and Reduced GFR to estimate Total Population Prevalence. It is likely that the higher than expected prevalence of CKD by CKD EPI and albuminuria has led to the finding of 21.9% in the population. This would not be concordant with other population based studies and is more typical of prevalence estimates from patients within the health system. Would the authors please comment on this with reference to existing studies?

Minor Essential Revisions

1. The authors might consider changing the title of the manuscript to more accurately to reflect the population sampled and the inferences that can be made to the general Irish population (E.g. Prevalence of Reduced Kidney Function in Middle and Older Age Subjects in the Irish Population).

2. Were smoking behaviour and physical activity considered in the analyses shown in Table 6? I note there is little commentary on the importance of the findings from Table 6 in the discussion section.

3. I would correct typographical errors (e.g. Abstract: Background: the prevalence of chronic kidney disease using available estimating equations within the republic of Ireland is unknown).

Discretionary Revisions

1. Given the body of literature that has consistently demonstrated poor performance of the MDRD vs CKD-EPI for higher GFRs, one might be inclined to remove this from the abstract but refer to it in the body of manuscript.

2. The abstract could be streamlined and the methods section condensed.

3. Would the authors consider reducing the number of tables in the manuscript? For example Tables 4 and 5 could be consolidated.

4. I would suggest that Figure 1 be removed from the manuscript as it does not add substantively to the manuscript.

**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'