Reviewer's report

Title: The assessment of renal function in relation to the use of drugs in elderly in nursing homes; a cohort study

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Reviewer: Ahsan Alam

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The article by Modig et al. describes the cross-sectional association between estimated GFR in elderly nursing home subjects and selected medication classes that are considered to be ‘renal risk drugs’.

The topic is of clinical importance due to the adverse events associated with inappropriate medication use, particularly in the elderly. The authors conclude that serum creatinine alone is insufficient in assessing kidney function for the purpose of drug prescribing, and the use of an estimating equation should be used; however, there is poor concordance between 3 equations that were studied (Cockcroft-Gault, MDRD, and a cystatin C-based equation).

Overall the authors’ conclusions are not novel and have been previously well appreciated. Some methodological concerns are also apparent and I have offered some comments below:

Major Compulsory Revisions:

1. It would appear that a single serum creatinine measurement was used to determine GFR? A single measurement may misclassify those with acute kidney injury or with a spurious creatinine value. How did the authors determine that this value was a ‘stable’ creatinine value for the patient? If a prior or repeat creatinine was not available this should be highlighted in the limitation section.

2. What were the inclusion/exclusion criteria for the study population? Were all those in the SHADES study included? Please provide a reference on page 5 (Study Population) for the detailed methods of the SHADES study.

3. An important factor in evaluating creatinine-based GFR equations is the standardization of serum creatinine. Were serum creatinine values performed in a single laboratory? Was the lab using a creatinine calibrated to an IDMS standard? If not, this should be stated in the methods, and commented on in the discussion as a possible source of bias.

4. Electronic reporting of estimated GFR (eGFR) has been implemented in many regions. Please comment whether eGFR reporting was available to the communities studied, and if so, which eGFR equation was used.

5. The Cockcroft-Gault equation, unlike the MDRD, is not adjusted for body surface area (BSA). It would appear that CrCl reported in the paper is in ml/min,
but this should be adjusted for BSA and be reported as ml/min/1.73 m2 in order to make appropriate comparisons with MDRD. I suspect this would change the degree of correlation between the 2 formulas.

6. The MDRD formula is biased at higher GFR (>60 ml/min/1.73 m2) while the Crockcroft-Gault CrCl usually overestimates GFR in those with low GFR. A more recent estimating equation has been developed (CKD-EPI by Levey et al. Annals of Internal Medicine, 2009) and would be considered more accurate across the range of GFRs in this study. In the absence of a ‘gold standard’ of a directly measured GFR, I would suggest the authors also include the CKD-EPI formula as a less biased estimate of GFR and to advance the literature from the most current level of understanding.

7. Since serum creatinine generation is related to muscle mass, can the authors report body weight or BMI of the study population in table 1.

8. Cystatin C is influenced by cancer, steroid use, thyroid disease, and cigarette smoking. Were data regarding these variables available for the study population? If so please include in table 1 and discuss in the manuscript.

9. Can authors specify how the medication lists were interpreted? i.e. would a single or limited-time use of an NSAID be considered equivalent to being on it chronically?

10. The authors document the prevalence of medication use, but what is more relevant is the appropriate use of these drugs. As the authors state in the discussion, the use of ACEI/ARB is favored in CKD, and digoxin may be used with caution if dosing is adjusted to GFR. Can the authors provide details on attempts to adjust the drugs for renal dosing (i.e. dose appropriate for GFR)?

11. I would suggest the authors also discuss the cross-sectional nature of this study design in the limitations section. It is entirely possible that the incidence of renal risk drugs is much higher, but adverse events lead to drug modifications (or patient death) such that they are not captured in a prevalence study? What one may be capturing are those who tolerate being on these renal risk medications.

12. In the discussion (page 8) the authors state “The National Kidney Foundation does not recommend the use of the MDRD equation in individuals with unstable creatinine concentrations…” Although true, this may mislead readers, since this applies to all creatinine-based estimating equations (including the C-G formula). I would modify the sentence to reflect any creatinine-based estimating equation is unreliable when the patient is not in a steady state.

Minor Essential Revisions:

1. The range of eGFR for women in table 1 is reported as (18-20). This appears to be an error since the mean is 64.9.

2. Page 5 “…multiple ill elderly…” is an odd term. Does this mean elderly with multiple comorbidities?
3. Page 10 “...precautious...” should be “cautious”

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

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.