Reviewer's report

Title: Low level exposure to cadmium increases the risk of chronic kidney disease: analysis of the NHANES 1999-2006

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Reviewer: Roberto Minutolo

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The paper by Ferraro et al examine the association between blood and urinary cadmium concentration and the presence of impaired GFR and albuminuria. Authors suggest that cadmium exposure inducing even a moderate increase of blood and urinary levels may affect risk stratification for CKD and proteinuria. The paper is well written and results adequately discussed. Some aspects, however, should be clarified:

Authors did not report any reference supporting the cut-off of albuminuria used in the study. According to de Jong and Curhan (JASN Aug 2006; 17: 2120 - 2126.) the cut-off values adopted (#17 and #25 mg/g for males and females) are in the middle of the range usually defining “high-normal” albuminuria. Therefore, it is not clear if the albuminuria risk associated to cadmium exposure refers to microalbuminuria or High-normal albuminuria. In the first case the cut-off levels should be #20 and #30 mg/g in males and females respectively, while gender-specific limits to define high-normal category are #10 and #15 mg/g.

Can Authors exclude that association of blood cadmium levels and CKD could be merely dependent on the reduced GFR?

Greater details must to provided on the correction of serum creatinine. Form the reported formulas (page 5), it appears that in the 1999-2000 survey, measured creatinine was underestimated while it was overestimated in 2005-2006 survey. Is this true? Are these formulas derived from a calibration process? Please provide reference if this is the case. A further concern is related to urinary creatinine. Were the same formulas applied also for correcting creatinine measured in the urine specimens?

Throughout the text, data should be expressed not only with median but also with range or interquartile range as Authors did in Table 1.

I suggest deleting figures 3-6 since they depict the same results reported in the Tables 2 and 3.

To make more legible the results, I also suggest to condense tables 2 and 3 in a single Table. The same for tables 4 and 5. Furthermore, please report uniformly in the tables or in the text the range of quartiles for blood and urinary cadmium.

Level of interest: An article of outstanding merit and interest in its field
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