Reviewer's report

Title: The correlates of urinary albumin to creatinine ratio (ACR) in a high risk Australian Aboriginal community

Version: 2 Date: 27 January 2013

Reviewer: Alex Chang

Reviewer's report:

In this manuscript, the authors examine correlates of albuminuria as measured by ACR in an interesting high-risk Australian Aboriginal population.

Major Compulsory Revisions

In the introduction, the authors state the innovations of their study including measurement of novel risk factors and modelling outcomes around their median values as well as the use of factor analysis. While using some interesting analytical strategies, I am not clear the added value of using factor analysis to represent blood pressure and body mass instead of simply choosing systolic blood pressure or body mass index or waist circumference. This may just make it more challenging to understand for the reader.

An important point to consider is the use of sex-specific ACR cutpoints. Warram et al (JASN 1996) suggest using a cutpoint of 25-355ug/mg for men and 17-250 ug/mg for women since women have lower muscle mass and urinary creatinine excretion than men. Certainly others have used the cutpoints used the authors have and this likely is not too be too important since most of the analyses are sex and age-adjusted. However, they should make some mention of this rather than imply that female gender is associated with micro/macroalbuminuria. It would be interesting to know if this still holds true using sex-specific cutpoints of ACR.

Use of population attributable fraction is an interesting concept especially in this high-risk Aboriginal population. However, I do wonder about the validity of this analysis that the authors have conducted. They state that the "simultaneous presence of all the factors with significant independent associations predicted probabilities of ACR>=30 of about 90% and of ACR>=300mg/g of about 80%, in people by 45 years of age."

However, each of these factors could be closely associated with each other. For example, a PAF of 20% for obesity would imply that if this risk factor were eliminated from the population, 25% of cases would be eliminated after elimination of this risk factor.

This would hold true if these factors were not associated with each other.
However, it is likely that GGT, body mass factor, diabetes, and CRP are all correlated (probably mostly due to the body mass). Thus, summing these factors together for a combined population attributable fraction may overrepresent the true estimate.

Moreover, there should be causal relationships between purported risk factors and the disease in order to estimate population attributable fraction. Certainly, arguments could be made for the role of some of these factors. However, as the authors note, there is no proof of a causal relationship between serum albumin and albuminuria, and it may be the albuminuria that results in the lower serum albumin levels.

The authors acknowledge the limitations of the cross-sectional study, but should also mention the limitations of their analysis using population attributable fraction and possible misinterpretations. The authors mention urine albumin being measured by immoassay or HPLC in the introduction but do not make mention of this in the methods, so this makes this statement confusing.

I believe study and understanding of the risk factors of albuminuria in such a high-risk population are very interesting, but question if the methods used are appropriate in summing up population attributable fractions.

**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.