Reviewer's report

Title: Revisiting Racial Differences in ESRD due to ADPKD in the United States

Version: 1 Date: 30 Nov 2018

Reviewer: Ronald Perrone

Reviewer's report:

We had the pleasure to review the manuscript by Murphy, et al for its potential candidacy for BMC Nephrology. The manuscript was well-written and presented in a clear and concise fashion and describes an association between non-Hispanic black and earlier onset of ESRD using data from the USRDS. We have a few suggestions that we feel will improve the manuscript and improve its importance for the journal's readership.

1. Our largest concern regards the associational nature of the study and that one has to be very careful to interpret its results. The authors do a nice job of mentioning some of these issues during the limitations section but these issues should be emphasized elsewhere in the manuscript to avoid the reader over-interpreting the results. As the authors mention in the limitations, the earlier onset of ESRD in non-Hispanic blacks has many different potential explanations, including possible differential rates of pre-emptive transplantation in whites versus blacks. This explanation alone may be source of the differences seen and we feel this point deserves emphasis in other sections of the manuscript, particularly in the discussion and abstract.

2. Additionally, the authors nicely describe the several other potential explanations of their data including socio-economic differences across races, differences in use of renal imaging modalities in whites versus blacks, as well as potential other comorbidities such as hypertension, diabetes but also importantly sickle cell trait/disease and APOL1 risk alleles. We feel that this information needs to be stated explicitly in the abstract, and that the sentence "Until further data are available, it may be prudent to consider black race an additional risk factor for progression in ADPKD" (page 2, lines 26-28) should be stricken from the manuscript, as it is too strong of a conclusion given these limitations in the data.

3. Are the authors familiar with any data on differential rates of the different PKD mutations by race? We suspect this has not been studied given the relatively homogenous populations involved in the groups from which risk calculators were derived. If data does not exist, it would be worth emphasizing that this is an important area of future study. Related to this, we might suggest the word "expectation" in the last paragraph of the Introduction be changed to "assumption", as this may not be valid.
4. A lot of the conclusions vary based on what is entered as the primary diagnosis for ESRD on the 2728 form. Do the authors know of studies that have supported the reliability/accuracy of ADPKD being reported as the primary diagnosis (as compared with secondary diagnoses)? Also there is no option to enter 753.12, which is sometimes uses as a PKD diagnosis. This would obviously affect things greatly if there is evidence that nephrologists enter ADPKD as a later diagnosis following HTN or DM, or others.

5. We were surprised with the degree to which the decrease in ESRD secondary to ADPKD after adjusting for the stratification factor of year was lower in blacks (OR 0.38) when compared with other analyses such as the lower incidence of ESRD of 0.864 vs. 0.912 per 100,000. This was also dramatically different from the similar analyses after adjustment for year in the group with DM (OR 0.95). Can the authors explain this? It may require more clarity in the methods.

6. We don't understand the variability shown in Figure 2B. The denominator (population) doesn't change. Please clarify.

Overall, we feel that the strength of the conclusions with regard to non-Hispanic black having more rapid progression to ESRD be dampened considerably as they likely are much stronger statements as currently written than the results justify.

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