Author's response to reviews

Title: Increasing renal cell cancer among black Americans: an epidemiologic review

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Author's response to reviews: see over
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Dear Editor,

Thank you very much for the helpful review of our manuscript, “Rapidly increasing renal cell cancer among black Americans: an epidemiologic review” and for the opportunity to submit a revised manuscript.

We have revised our manuscript according to the suggestions of the reviewers, as indicated in detail below, and a revised manuscript with all changes marked has been submitted.

Please let me know if you have any questions.

Regards,

Loren Lipworth
Reviewer 1

This is an excellent review of epidemicologic factor of RCC, with a focus on blacks. Thank you.

Discretionary Revisions:
The title is somewhat misleading, since the incidence rate in black people in the US seems to have been stabilized between 2001-2006. And furthermore, the increase was found also in whites. Data from a recent European study, (Levi F, Ferlay J, Galeone C et al. The changing pattern of kidney cancer incidence and mortality in Europe. BJU Int 2008;101:949-958.) which analyzed kidney cancer incidence 1980-2004, indicate a shift towards stabilization or a decrease in incidence in recent years in both sexes. Also overall mortality rates for kidney cancer, in Europe, increased until the late 1980s/early 1990s, thereafter rates have stabilized or declined. In the EU, mortality rates from kidney cancer declined from a peak of 4.8 per 100,000 in 1990-1994 to 4.1 per 100,000 in 2000-2004 (−13.1%) in men, and declined from 2.1 to 1.8 per 100,000 (−17%) in women. This trend seems also visible in figure 2.

Although incidence rates do appear to have recently stabilized or decreased in many European countries, as demonstrated by Levi et al. and correctly pointed out by the reviewer, the same is not true in the United States, where incidence rates for renal cell cancer have been rising steadily each year. Nevertheless, we have changed the title to “Increasing renal cell cancer among black Americans: an epidemiologic review.”

With a lack of known occupational factors, life-style factors seems to be the major factors for RCC development. Whether there in general is a difference in life-style between races there are evidence that there are differences in life-style based on socioeconomic factors in Europe. Is there a similar economic situation between blacks and whites in the US? However, there is a need for detailed etiologic studies based on race in the US having a mixture of races and differences (?) in life-style.

We agree, as indicated in the manuscript, that renal cell cancer is not convincingly linked to any occupation. In general, no consistent association has been demonstrated between renal cell cancer and social class variables such as education or income, which we now indicate on page 4-5. Thus, we have emphasized that this review focuses largely on lifestyle factors, some of which may relate to socioeconomic status, and, as the reviewer suggests, that there is a strong need for detailed etiologic studies of renal cell cancer in blacks.

Reviewer 2

The submitted manuscript is worthy of publication provided some modifications and changes are made. As can be noted from the attached slides on Kidney Cancer (85% is RCC) in Florida, the Incidence data from the Florida Cancer Data System is some what
different than the SEER National data. In Florida, the incidence rates, although on the rise, they are lower in Blacks than Whites and early stage is only slightly higher in Blacks with more Black cases are unstaged than White cases. For 2004, incidence rate in Blacks is slightly lower (males and females) while mortality rate is slightly higher (males only).

**While the reviewer is correct that there may be slight geographic differences within the United States in the incidence and staging black-white trends, we believe that the overall nationwide SEER trends through 2007 present the most accurate picture of the descriptive epidemiology for the purposes of this general risk factor review.**

The claim in the methods section that ,”virtually no epidemiologic studies examining risk factors for renal cell cancer separately among Blacks,” is not accurate. However, the authors do note that small numbers of Black participants prevented presentation of data for Blacks separately. I do recommend that the authors review the three publications on a study completed in Florida that included Blacks and Whites and the data for Blacks is presented separately. Clearly the numbers for Blacks (73 cases and 71 controls) is somewhat small.

**Thank you for the citations. After carefully reviewing the three studies cited by the reviewer (although the paper by Asal et al. on obesity is not indexed in PubMed and we were able to access only the abstract and first page), we believe that our statement that ”virtually no epidemiologic studies examining risk factors for renal cell cancer separately among Blacks” is in fact accurate. The publications referred to by the reviewer include 73 black cases and 71 black controls, but no ORs are presented separately for blacks for any risk factors evaluated in any of the three papers. Nevertheless, we have now cited the three publications among multiethnic studies conducted to date (page 6), and we have revised the statement in the manuscript to clarify that “there have been virtually no epidemiologic studies presenting results for lifestyle risk factors for renal cell cancer separately among blacks.”**

The Results sections on Genetic Susceptibility and Chronic Renal Disease are excellent. The section on obesity, Cigarette Smoking, and Diet could be improved by incorporating findings from the 3 attached references especially the association between environmental tobacco smoke and RCC in Blacks, more refined measures of obesity as reported separately for Blacks and Whites, and the protective effect between RCC and vegetables, broccoli, vitamins A, C, D, K, calcium, iron, potassium and zinc that are present in whites but not in Blacks. Also the increase risk associated with intake of Fried meats, hot dogs, and lunch meat that is present in Blacks as well as Dairy products.

**See above. We are unaware of published results from the three cited references that are reported separately for blacks.**

The Conclusion section should also be modified to reflect recent findings on the association
between Obesity, body composition, and environmental tobacco smoke in Blacks.

See above.

Reviewer 3

This is a review of risk factors for renal cell carcinoma with particular attention paid to risk disparities in exposures to risk factors that would explain the increased incidence of renal cell carcinoma among African Americans. The review of RCC risk factors is competent. Unfortunately, few studies have investigated RCC risk factors by race, which weakens the rationale for the article.

While data on RCC risk factors among blacks are limited, as we acknowledge, we have reviewed all relevant studies (including studies pointed out by reviewer 2) and attempted to put the available data in the context of the descriptive trends. Most importantly, we emphasize the need for, and hope to guide in some way, further etiologic studies among blacks in light of these descriptive trends and the patterns of known or suspected risk factors among blacks and whites.

Major Compulsory Revisions:
(1) The authors refer to the increased incidence among African Americans and the equivalent mortality between African Americans and Caucasians as "paradoxical." I do not think that these two trends qualify as a paradox, even considering lower rates of nephrectomy among African Americans; the authors should use less dramatic language that better describes the incidence and mortality differences seen between the races in RCC.

We have revised our language in the discussion of trends in the Introduction and Conclusion.

(2) The authors state, "This excess is unexpected since early stage renal cell cancer is primarily detected incidentally by imaging modalities which are generally thought to be utilized less frequently by blacks than whites." This statement could use a reference, but more importantly, this hypothesis could use some investigation. The authors suggest that increased abdominal imaging may account for the observed pattern of increased incidence but unchanged mortality among African Americans. Abdominal imaging by race would certainly be helpful in assessing the prevalence of incidental diagnoses of RCC. If that is unavailable, then an evaluation of the prevalence of abdominal conditions by race that may lead to abdominal imaging may be helpful. In a manuscript focused on racial differences in incidence rates of RCC, a review of abdominal imaging by race is probably as important as a review of RCC risk factors by race, particularly if localized cancers make up the bulk of the excess cancers among African Americans.

We agree with the reviewer; unfortunately, despite numerous searches, specific data on abdominal imaging by race are unavailable. We have revised the manuscript.
(page 4) to clarify that the difference in early stage renal cell cancer was evident as early as the 1970s, and that we believe it is implausible that blacks had greater access to imaging technology 40 years ago. We suggest, rather, that the difference may reflect a difference in the biology of renal cell cancer in blacks.

Reviewer 4

There are no major revisions. I thought this was well written and covered the major areas of interest in the field. The only concern I have is the fact that the authors reviewed potential causes for RCC development yet not sure that is what the title really means. Just by reading the title I was expecting to see an epidemiological review of RCC in black americans yet I encountered a series of possible etiologies linked one way or another to RCC in blacks. I think it would have been more useful to simply review whatever data exists *if any) on black and RCC only rather than going thorough the entire cause-effect type of approach. Despite of this I think this is a very informative manuscript that deserves publication.

Thank you.

The impetus for this review was the observed striking patterns in the descriptive epidemiology of renal cell cancer in blacks and whites. While the reviewer is correct that we have reviewed all relevant studies, there are virtually no studies specifically among blacks; we have attempted to put the available data in the context of the descriptive trends, particularly the higher incidence among blacks, as well as black-white trends in known or suspected risk factors for renal cell cancer. Most importantly, we emphasize the need for, and hope to guide in some way, further etiologic studies among blacks in light of these descriptive trends and the patterns of known or suspected risk factors among blacks and whites. We have, as indicated in our response to reviewer 1 above, slightly modified our title.