Author's response to reviews

Title: Smoking, environmental tobacco smoke and risk of renal cell cancer: a population-based case-control study

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

Attached please find our revision of the following original research article, “Smoking, environmental tobacco smoke, and risk of renal cell cancer: a population-based case-control study,” which is being considered for publication in the journal *BMC Cancer*.

We are appreciative of the reviewers’ comments and have made efforts to address each of their concerns in the revised manuscript. Following is a point-by-point summary of changes we have made to this manuscript.

**Ethical approval / informed consent**

- The official designation of the University of Florida Institutional Review Board (UF IRB-01) and acknowledgment that subjects provided informed consent have been added to the revised manuscript, page 6.

**Reviewer: Alexander Parker**

- We recognize Dr. Parker’s concern that all histologic subtypes of renal cell cancer were included in our case group. A paragraph has been added to the discussion section (pg. 17), acknowledging the limitations posed by including all histologic subtypes in a case-control study of RCC. Two references were added to support our statement (Chow et al. 2008, Cheville et al. 2003).

- The wording of our statement regarding confounding of inhalation findings (pg. 9) has been changed to address Dr. Parker’s concern about the statistical accuracy of our statement. The change acknowledges that it is attenuation of the association, rather than loss of statistical significance, that suggests confounding by dose.

**Reviewer: Paolo Vineis**

- The low response rate among controls in our study (42%) is considered a major limitation. Following Dr. Vineis’ suggestion, we have added estimates on lifetime ETS exposure among teachers in California (Reynolds et al. 2004) to compare with our findings. Currently, there are few studies that present population-level
prevalence of lifetime ETS exposure in the United States. (Most studies present prevalence of current, rather than lifetime ETS exposure.) While the sample studied by Reynolds et al. (2004) does not represent precisely the same population as our study, we feel that this reference provides the most appropriate estimates for comparison available at this time. Our estimates for home ETS exposure among controls were found to be slightly lower than those presented by Reynolds et al. (2004), suggesting that selection bias may have been present and that our odds ratios for home ETS are over-estimated. However, we believe that this potential overestimation is slight, and does not affect our conclusion that ETS exposure in the home is a likely risk factor for renal cell cancer. These changes have been made on page 16 of the revised manuscript.

- We recognize that hypertension is an important risk factor for renal cell cancer. History of hypertension was collected by self-report in epidemiologic interviews. However, no associations between hypertension and renal cell cancer were found, which we suspect was due to misclassification of subjects who claimed to be hypertensive by self-report, but were never formally diagnosed. This point has been added to page 8 of the revised manuscript.

Overall, we believe that the reviewers’ suggestions have improved upon this manuscript, particularly in reference to understanding how low response rates may have affected our ETS estimates. We thank you for your consideration of this manuscript and look forward to a final decision.

Sincerely,

Ryan Theis, M.P.H.