Author's response to reviews

Title: Risk of urinary bladder cancer: a case-control analysis of industry and occupation

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Author's response to reviews: see over
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Melissa Norton, MD
Editor-in-Chief
BMC Cancer

Dear Dr. Norton,

MS: 1087001457298138

We are grateful for the reviewer’s constructive comments of our manuscript "Risk of urinary bladder cancer: a case-control analysis of industry and occupation." We have addressed the reviewer’s specific comments below and revised our manuscript accordingly.

1. The authors have written a very nice manuscript based on a large case-controlled study. However, it is unclear what the implications of the authors’ findings are. Increased risk of bladder cancer was discovered in widely disparate occupations: waiters, communications, medical specialists and livestock workers. Do the authors believe that their is a causative agent in each of these occupations or are their findings a statistical anomaly? For example, I am not sure that an increased risk in health care workers is related to their awareness of signs and symptoms of bladder cancer and thus an earlier diagnosis, as the authors suggest. While health care workers may indeed be diagnosed at an earlier stage—if they do immediately get evaluated for hematuria and dysuria—but not necessarily in a greater percentage than the non-medical population. The authors should more robustly discuss that varying nature of their findings and the fact that further investigations are clearly warranted in specific occupations. That being said, it would be difficult to label any occupation as increased risk based on this data.

Because analyses by occupation and industry code lack a true exposure orientation, we were not able to assess the causative agent in this study. However, we attempted to compensate for this by discussing possible causative agents, which have also been reported in previous studies. It is also true that statistically significant associations may be a chance finding, and we have discussed this as one of the limitations of our study. As suggested, we have more robustly discussed our finding of excess risk in medicine and health occupations, and in the health services industry. In particular, we have included an additional paragraph on sedentary work or frequency of urination as a risk factor for UBC (page 10, lines 6-13). For consistency, we have followed with the paragraph on UBC risk in waiters and bartenders, which discusses fluid intake as a risk factor for UBC. The paragraph on electrical assembly, installation, and repair, and communication industries has been revised (page 11, lines 3-13), and we have included a new paragraph on structural work and bench work (page 11, lines 14-21). References have been reordered, and are presented in accordance with the journal requirements.
2. The authors should also address why certain professions has reduced risk of bladder cancer for those employed less than 10 years, however, significantly increased risks for employment greater than 10 years (e.g., farmers). Clearly, risk (if there is a true cause-and-effect correlation) should be based on a continuum, such that as time increases, risk increases. Obviously, with such small numbers of subjects (26 and 17), the statistical and clinical significance becomes questionable.

We thank the reviewer for highlighting these important issues. We have included a sentence suggesting that observed associations may have occurred by chance because of multiple comparisons (page 12, lines 4-5), and that cautious interpretation of the results is warranted (page 12, line 9). Also, we discuss the implication of increased risk of UBC with duration of employment (page 12, lines 11-14)

3. Furthermore, with such small numbers in each specific occupation as well as a very unbalanced sample of smokers and non-smokers (73% vs. 53%), statistical significance may not infer clinical significance.

We have acknowledged that the small number of people in occupation and industry groups is a limitation - similar in many respects to other case-control studies of occupation. We collected complete data on the smoking habits of patients and controls, which enabled adjustment of our risk estimates for cigarette smoking. Therefore, this cannot fully explain the significantly increased risk of urinary bladder cancer that we observed in several occupations and industries. Nevertheless, we have been careful to indicate that further investigation is warranted to explore putative associations between occupation, industry and urinary bladder cancer.

4. The number of General farmers in the text is different from that in the table. Please check it again.

We are grateful to the reviewer for spotting our mistake, which we have corrected (page 7, lines 14-17).

We trust that these revisions meet with your approval, and we respectfully submit our revised manuscript to be considered for publication in BMC Cancer. Should you require any further information, please do not hesitate to contact me.

Sincerely,

Jie Lin, Ph.D.
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