Author's response to reviews

Title: Regular Aspirin Use and Lung Cancer Risk

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To Whom It May Concern:

We were pleased to learn that you would consider our manuscript titled "Regular Aspirin Use and Lung Cancer Risk" for publication in BMC Cancer after addressing Prof. Harris' comments. All authors agree that these comments were quite thoughtful and that the final manuscript will benefit from the reviewers input. Please find below our item by item response to the reviewers comments:

1. We have corrected the percentages referring to the odds ratios associated with tablet years. As pointed out by the reviewer the risk reductions were 37 and 55% respectively. We added the risk estimates for non-small cell lung cancer to the abstract, result section, discussion and Table 5. As expected, we observed significant risk reductions for both NSCLC and SCLC.

2. As outlined in our methods section, none of our control participants suffered from malignant or benign tumors. The control participants came to our institute for a suspicion of neoplastic disease or other medical services, but were not diagnosed with cancer or benign conditions.

3. We are in complete agreement with Prof. Harris that our study may be biased due to the fact that we could not evaluate the effect of other NSAIDs. Our data set includes reliable information on acetaminophen. We saw no association between acetaminophen use and risk and chose not to include these findings in the current manuscript, due to comprehensiveness of data already presented. We felt that the inclusion of these null results would distract from the aspirin findings, rather than add to the manuscript, especially in light of the fact that there is no clear biological mechanism by which acetaminophen would influence lung cancer risk. Our data set also include some information on other NSAIDs, such as ibuprofen. However, questions regarding use of ibuprofen have been added to the instrument at a later time. Thus, reliable data for this agent is missing for most study participants (cases and controls alike) and we decided that it would not be appropriate to include these sketchy data.
elements into our current analyses. We did however add a brief discussion on the potential source of bias associated with the lack of data on other NSAIDs to our discussion section.

4. As mentioned in our response to item #2, all of our controls were non-cancer controls. Thus a stratified analysis is not necessary. We included the pooled risk estimate for all NSCLC cases in table 5, the abstract, and the text of the manuscript. Consistent with Prof Harris' expectation, there was a significant NSCLC risk reduction associated with regular aspirin use.

5. Again, this study did not utilize cancer controls.

6. We changed the explanation of the Rosenberg et al. results to "Non-significant risk reduction associated with aspirin use when case group compared to cancer controls (RR=0.80; 95% CI 0.60-1.20), but not apparent when compared to non-cancer controls (RR=1.00; 95% CI 0.70-1.40)". Pooled results for NSCLC cases are presented in Table 5.

Please do not hesitate to contact me if you should require any further information regarding this manuscript.

Sincerely,

Kirsten B. Moysich, Ph.D.
Assistant Professor