Reviewer’s report

Title: Low-moderate arsenic exposure and respiratory health in American Indian communities in the Strong Heart Study

Version: 0 Date: 11 Aug 2019

Reviewer: John Balmes

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GENERAL COMMENTS
Overall, this is a clearly written manuscript that reports associations between urinary arsenic concentrations and spirometric lung function in a large cohort of American Indians. The manuscript has a number of strengths, including the unique study population, sample size, use of study-specific spirometric reference values, careful statistical analysis, and adjustment for appropriate covariates, especially smoking. Despite these strengths, there are several limitations. Post-bronchodilator spirometry was not done, meaning that COPD cannot be properly assessed. Self-report of emphysema and chronic bronchitis is prone to outcome misclassification as the authors note. The relative inconsistency between the association of urinary arsenic concentration with odds of shortness of breath and that with the odds of having to stop because of shortness of breath is also problematic, suggesting potential participant misunderstanding of the symptom questions. In fact, the relative lack of association of most respiratory symptoms with urinary arsenic concentrations and the significant protective association with cough suggest that any effects of the low-moderate level arsenic exposure in this population are not of clinical importance. This interpretation is also supported by the small differences in lung function observed between 25th and 75th percentiles of urinary arsenic concentration. The Discussion section should be revised to include mention of the limited clinical significance of the findings.

SPECIFIC COMMENTS
Lines 11-112 As noted above, airway obstruction cannot be properly classified as COPD without post-bronchodilator spirometry. This should be acknowledged as a limitation in the Discussion.

Line 149 "Mycobacterium" is one word.

Line 234 "People" or "individuals" would be better than "patients" here.

Line 249 Because no post-BD spirometry was done, "COPD" should be replace by "airflow obstruction."

Line 249 What is the basis for the assertion that "diabetes could be on the causal pathway between arsenic and restrictive lung pattern"? More explanation of the authors' reasoning would be helpful.

Lines 296-297 "select respiratory symptoms" is a bit misleading given the conflicting nature of some
of the authors' results. Specifically listing "stopping for breath" as is done in the Conclusions of the Abstract would be better.

**Level of interest**
Please indicate how interesting you found the manuscript:
An article whose findings are important to those with closely related research interests

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Please indicate the quality of language in the manuscript:
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