Author’s response to reviews

Title: Directly measured secondhand smoke exposure and COPD health outcomes

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Author's response to reviews:

Re: manuscript 4587317779836880

May 18, 2006

Dear Dr. Hodgkinson-Barrett:

Thank you very much for the thoughtful review of our manuscript. We have revised the manuscript in accordance with the reviewer's suggestions and address each of their points below.

REVIEWER 1

Minor essential revisions.

Point 1. The reviewer indicated that we could omit the statement that respondents who reported asthma alone were not considered for the study. We have done as the reviewer suggested.

Point 2. The reviewer provided a comment about the denominator of the 47 subjects for whom we had validation with spirometry. We have revised the Methods (p.4) to indicate this point: "As reported previously, we validated the case definition of COPD using spirometry in a subgroup of 47 participants with COPD whose physicians provided spirometry reports (of 386 subjects)."

Major compulsory revisions.

Point 1. The reviewer indicated that we should clarify why study waves 3 and 4 were used for this manuscript. We have revised the Methods (p.5) to clarify that direct SHS monitoring was only carried out in study waves 3 and 4: "We used data from wave 3 and wave 4 of a population-based multi-wave longitudinal cohort study of U.S. adults to elucidate the impact of SHS exposure on COPD health outcomes. Direct measures of SHS exposure were obtained only in these waves."

Point 2. The reviewer provided a comment asking whether the new cases of COPD identified in each successive wave represent incident cases. We believe that this is likely, but further discussion of this issue is beyond the scope of the current manuscript. A dynamic multi-wave analysis of incident COPD is planned as the subject of another manuscript.

Point 3. The reviewer indicated that more discussion of the issue of selection bias would be helpful to the reader. We had previously acknowledged in the Discussion the possibility of selection bias. To address this possibility, we compared the baseline characteristics of subjects who did and did not participate in the direct SHS monitoring and found no statistical differences (Table 1). To further address the issue of possible selection bias, we used multivariate logistic regression analysis to develop sampling weights to account for non-participation. We then repeated key analyses with the sampling weights and found no substantive differences compared to the primary analysis. This supports the absence of significant selection bias in the study.
To indicate these points, we revised the Methods (p.10): "As above, participants in the direct SHS monitoring program were similar to non-participants, including socioeconomic status, COPD severity, and physical health status. To further take non-response into account, sampling weights were developed using all the personal characteristics in Table 1. The weighted analysis was not substantively different from the unweighted analysis, so we report the unweighted analysis only."

We also revised the Discussion (p.16) to further indicate this point: "However, the similarity of participants and non-participants reduced the likelihood of this potential bias. In addition, incorporating sample weights that account for non-response into the analysis had a negligible impact on study results (data not shown)."

Point 4. The reviewer provided a comment about statistical power. We had previously acknowledged this limitation in the Discussion (p.16): "The other consequence of lower study participation is diminished statistical power, which resulted in decreased precision of effect estimates. In some cases, there appeared to be a negative effect of SHS exposure, but the 95% confidence intervals were wide and included no association. A larger sample size might have resulted in clearer evidence of SHS effects in these cases and would be required to detect smaller effects."

In addition, the reviewer suggested that a post-hoc power calculation be carried out. We agree with the position of Goodman and Berlin that reporting the 95% confidence intervals is a better way of conveying the precision of results than post-hoc power calculations (Goodman SN, Berlin JA. The use of predicted confidence intervals when planning experiments and the misuse of power when interpreting results. Annals of Internal Medicine 1994; 121:200-6). If editorial priorities dictate, we would nonetheless be willing to provide such a calculation.

Point 5. The reviewer indicated that further comment about why the 3 exposure measurements are not strongly correlated among each other would be helpful to the reader. We have revised the Discussion (p.15) to clarify this point (the last sentence was added): "The results differed somewhat depending on the method used to measure SHS exposure. For self-reported exposure, the overall pattern of results suggested a deleterious effect of SHS exposure on COPD-related health status, but the estimates were imprecise in many cases. This is probably attributable to the lower accuracy of self-reported SHS exposure. When urine cotinine was examined, which is an objective and specific measure of SHS exposure, the association between higher SHS exposure and poorer COPD-related health status was most clearly demonstrated. Personal badge nicotine levels, in contrast, were not associated with any health status variable. The different results for urine cotinine and personal badge nicotine levels may indicate that peak SHS exposure, rather than average SHS exposure, is more relevant to disease severity and health status in COPD. Personal badge data represent an integrated average exposure to nicotine during the time period that the badge is worn, whereas urinary cotinine data are more reflective of recent peak exposures. Alternatively, the personal nicotine badge measurements may have been subject to greater exposure misclassification than urine cotinine, because correct measurement depended on subjects reliably wearing the badge during all their daily activities (whereas urine cotinine was not). These methodologic differences likely also account for the low correlation among measures."

Point 6. The reviewer pointed out an error in the legend of Table 3. This has been corrected.

Point 7. The reviewer provided another comment about sample size and power. Please see the response to point 4.

REVIEWER 2

Minor essential revisions.

Point 1. The reviewer pointed out that the AQ-20 is distinct from the St George Respiratory Questionnaire. We have revised the Methods (p.) to clarify that the origin and validation of the AQ-20: "We used the Airways Questionnaire 20 (AQ-20) to measure disease specific quality of life.[32] This instrument is a short survey that was validated against the St. George’s Respiratory Questionnaire, which is a 50 item instrument that has been used extensively in COPD to measure disease-specific QOL.[33, 34] It has excellent psychometric properties for assessing QOL in COPD and asthma and higher scores correspond to poorer QOL.[32, 35]"

Point 2. The reviewer commented that the relationship between self-reported and directly measured SHS
exposure would be helpful to the reader. To address this comment, we have revised the Methods (p.12) to indicate that these results are in the legend for Table 2: “Table 2 shows the distribution of exposure for self-reported and directly measured SHS exposure. The table also shows the inter-relationship between the SHS measures (legend)."

Point 3. The reviewer pointed out a typographical error. We have corrected it.

Point 4. The reviewer pointed out an incorrect reference, which we have now corrected.

GENERAL EDITORIAL CHANGES

We have made the requested changes. There are 3 tables in landscape format which are too wide to re-format in portrait. Will this be acceptable? Otherwise, we may have to delete the bivariate analysis columns. Please advise.

Thank you very much for the opportunity to revise our manuscript. Please let us know if any additional changes are required. We look forward to hearing from you.

Sincerely,

Mark D. Eisner, MD, MPH
Corresponding Author