Author's response to reviews

Title: Adverse Childhood Experiences are Associated with the Risk of Lung Cancer: A Prospective Cohort Study

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A Prospective Cohort Study”

1. Reviewers 2 and 3 had no additional comments.

2. Per suggestions from Reviewer 1, we have included a table with descriptive statistics of the study population. Following on comments from Reviewers 1 and 4, we have removed the confidence interval functions and related text. A list of tables and figures in the revised manuscript follows.

- Table 1. Select characteristics of ACE Study participants at baseline (new)

- Table 2. Definition and age-standardized prevalence of adverse childhood experiences (ACEs) at baseline by smoking: Kaiser Permanente, San Diego, California, 1995-1997 (formerly Table 1)

- Table 3. Association between number of categories of adverse childhood experiences (ACEs) and the prevalence and risk of selected smoking behaviors among 17,337 adults (formerly Table 2)

- Table 4. Frequency, age-adjusted risk, and risk ratio of the occurrence of lung cancer, identified by hospital discharge records, between baseline and 31 December 2005 by number of categories of adverse childhood experiences (ACEs) and smoking status among 15,365 adults (formerly Figure 2)

- Table 5. Frequency, age-adjusted risk, and risk ratio of the occurrence of lung cancer, identified by death records, between baseline and 31 December 2005 by number of categories of adverse childhood experiences (ACEs) and smoking status among 16,901 adults (formerly Figure 4)

- Table 6. Frequency, age-adjusted risk, and risk ratio of the occurrence of lung cancer, identified by hospital or death records, between baseline and 31 December 2005 by
number of categories of adverse childhood experiences (ACEs) and smoking status among 16,901 adults (formerly Figure 5)

3. Regarding Reviewer 4’s comment on the target journal, we had thought this manuscript was submitted to BMC Public Health for consideration; thus, the comment regarding BMC Medicine is not clear. Nonetheless, we agree that BMC Public Health is the appropriate target.

4. We agree with the Reviewer that “[t]reatment of potential mediators is a very troublesome exercise and there is considerable disagreement among epidemiologists about the correct approach”; however, we disagree that the approach (a common one) we have taken is “weak and unconvincing”. This a matter for continued debate and we appreciate the Reviewer’s time in describing the recent approach by MacKinnon.

5. We disagree with the Reviewer regarding the notion that “[a]ttibutable risk is a tenuous concept…” and recall that the Reviewer has published on the topic (Stellman SD, Garfinkel L. Proportions of cancer deaths attributable to cigarette smoking in women. Women Health. 1989;15(2):19-28.), albeit 20 years ago and we recognize views change over time – we know that our views have changed. Regardless, we have removed the sections addressing attributable risk and will discuss this elsewhere. Our action is not based on the Reviewer’s comment; rather we feel that much more discussion is needed than can be given here on the need to consider risk factors for risk factors in regards to attributable risk.

6. We have removed Figure 3; however, we have left a brief description in the average age at hospitalization and at death in the text with the following addition to the text: “Of course, comparisons of average-at-hospitalization across groups are not straightforward since the average age-at-hospitalization depends to a large extent on the age distribution of the underlying groups being compared.”