Author's response to reviews

Title: Indoor Air Pollution Exposure from Use of Indoor Stoves and Fireplaces in Association with Breast Cancer: A Case-Control Study

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Author's response to reviews: see over
White AJ, et al. Indoor Air Pollution Exposure from Use of Indoor Stoves and Fireplaces in Association with Breast Cancer: A Case-Control Study

Environmental Health Review, Revision 2

Reviewer 1: Jennifer Peel

Reviewer’s report:
I thank the authors for their responsive revisions to the reviews. The manuscript is much improved, but I have just a few remaining questions.

RESPONSE: We are glad to hear the reviewer found our revisions responsive and have addressed their remaining concerns below.

REVIEWER 1: Specific Comments:

REVIEWER 1, COMMENT 1. Although I think PAHs are most certainly a strong possible driver of the observed association, and should be discussed as such in the manuscript (e.g., in the Discussion), the fact remains that the authors did not assess PAHs in this study. Additionally - there are likely other chemicals in the emissions that could plausibly be carcinogenic. I continue to think that the focus on PAHs should be reduced. For example - in the Abstract: “However, the association between PAHs from indoor stove/fireplace use and breast cancer risk is unknown.” This statement is misleading and misplaced because this is not the association being evaluated in this study. At the very least the authors should provide further justification of the focus on PAHs; there is much information provided about PAHs, but little regarding the other chemicals in emissions (particularly in synthetic logs during the relevant time period for this study) (e.g., evidence that these other chemicals are not likely to cause cancer).

RESPONSE: We have removed PAHs from the statement in the abstract (Page 3 of the revised manuscript) and have expanded on a statement in the discussion acknowledging other the other chemicals in synthetic logs (Page 17 of revised manuscript) as follows:

“For example, synthetic logs may emit polychlorinated biphenyls, particulate matter, polychlorinated dibenzodioxins and dibenzofurans, hexachlorobenzene, carbon monoxide, nitrogen oxides, volatile organic compounds and formaldehyde (Gullett et al. 2003; Li and Rosenthal 2006; McDonald et al. 2000). However, none of these chemicals have been found to be consistently associated with breast cancer risk as is the case for PAHs across different exposure sources (IOM (Institute of Medicine) 2012).”

REVIEWER 1, COMMENT 2. I thank the authors for adding Table 1. It seems unnecessarily busy. I think 2 tables (one by case control status and one by exposure status) would be clearer to the reader. There are some important differences between cases and controls that are difficult to discern in this format.

RESPONSE: We appreciate your comment. However, we have already published detailed study characteristics by case-control status and have referenced that publication (Gammon et al. 2002) in this manuscript. Replication of already published data (distributions of potential covariates by case-control status), given the current restraints on journal space and copyright concerns, doesn’t seem prudent. Thus, we instead chose to present new data, which includes the relevant covariates stratified by exposure level and case-control status. This new information augments the information previously published in Gammon et al. 2002 (which only
helps a reader to assess potential risk factors for breast cancer), and improves the readers’ ability to judge which factors may be potential confounders and thus of concern in the study presented here (because we now show which potential breast cancer risk factors are associated with the exposure). The alternative presentation we elected to illustrate in Table 1 therefore optimizes the readers’ ability to adequately evaluate our study data and approach.

**REVIEWER 1, COMMENT 3.** I am concerned about a potential source of misclassification of the exposure, but I’m not sure that I understand the study clearly. It appears to me that (in the main analysis) if a woman lived outside of Long Island and used a fireplace that exposure is not captured in any of the measures that were examined in this manuscript. If that is correct, it seems like we would like to know if cases and controls differed with respect to their length of residence on Long Island in order to know if this misclassification is potentially differential (and therefore could lead to a bias away from the null).

**RESPONSE:** This is correct – any exposure that occurred at a non-Long Island residence was not captured by the exposure assessment. Study participant characteristics by long-term resident status have been previously published (Gammon et al. 2002). To address this possibility, in our original submission, we provided results of an analysis limited to those who were long-time residents of Long Island (≥15 years in the same home) and found associations to be similar (Additional File 1, discussed in text on Page 12). We have now amended the manuscript (Page 12 of the revised manuscript) to clearly acknowledge that there are differences among women who were long-term residents on LI, and we cited our previously published paper that displays those differences.

“Study participant characteristics have been previously found to differ by whether or not the respondents reported living in the same home for 15 years or more (Gammon et al., 2002). However, a sensitivity analysis restricted to long-term Long Island residents found a similar trend among any stove/fireplace use and wood users and an increasing trend for women burning synthetic logs for 19 years or longer (see Additional File 1”

**REVIEWER 1, COMMENT 4.** With regard to possible selection bias – participation/response rates often vary by socioeconomic status, as does fireplace use.

**RESPONSE:** While it is possible that participation rates may have varied by socioeconomic status, cases and controls had similar distributions of income and education (as previously published in Gammon et al., 2002). Additionally, stove/fireplace use is more common among low-income populations whereas high socioeconomic status is a risk factor for breast cancer. Thus, stove/fireplace use is not a proxy for the risk factor, high socioeconomic status. We have addressed this concern on Page 18 of the revised manuscript as follows:

“Participations rates may vary by socioeconomic status. High socioeconomic status is a risk factor for breast cancer (American Cancer Society 2013-2014); however, indoor stove/fireplace use is more common in low-income populations (Rogalsky et al. 2014). Thus, it is unlikely that stove/fireplace use is a proxy for socioeconomic status.”

**REVIEWER 1, COMMENT 5.** Residual confounding can also be present when measured confounders are not measured well (e.g., alcohol intake or physical activity). I suggest adding a statement to acknowledge the possibility.

**RESPONSE:** Residual confounding from imprecise measurement of confounders is always a possibility in an epidemiologic observational study. (However, please note, to assess
life course alcohol intake and recreational physical activity in the LIBCSP, state of the art instruments were employed (McCullough et al. 2012; Terry et al. 2006). We have amended the discussion to more precisely address this (page 19 of the revised manuscript), as follows.

“There was also little existing literature on predictors of stove/fireplace use. Therefore, residual confounding may be present, either by lack of inclusion of a confounder or by imprecise measurement of a confounder included in the model. However, we included many known breast cancer risk factors in our adjustment sets in order to mitigate this concern.”

Level of interest:
An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests: I declare that I have no competing interests

REVIEWER 2: Linda Birnbaum

Reviewer's report: This paper is now acceptable for publication

RESPONSE: We thank the reviewer for considering the revised manuscript and finding it suitable for publication.
References


Li VS, Rosenthal S. 2006. Content and emission characteristics of Artificial Wax Firelogs Omni Environmental Services for EPA Reg 5 / Environment Canada


