Author’s response to reviews

Title: State of the evidence 2017: An update on the connection between breast cancer and the environment

Authors:
Janet Gray (grayj@vassar.edu)
Sharima Rasanayagam (srasanayagam@breastcancerfund.org)
Connie Engel (cengel@breastcancerfund.org)
Jeanne Rizzo (jeanne@breastcancerfund.org)

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Reply to reviewers: EHNE-D-16-00286

First I would like to thank the reviewer for her careful reading of our manuscript and for her thoughtful suggestions for making the report stronger. We have implemented her suggestions, both structural and more detailed, and we believe the manuscript is far improved for having made these changes.

Revisions since our original submission of EHNE-D-16-00286, ‘State of the Evidence 2017: An update on the connection between breast cancer and the environment’, are indicated in yellow highlight in the revised manuscript.

Major revisions include:

• In the introduction, we have included a brief preview of the paper’s organization (lines 63-73).

• We have added a full section on our methods for selecting articles for inclusion in this review, including search terms and dates, and a brief statement on adjustments and interactions reported in the individual reports’ statistical results. We also acknowledge that we report negative findings, as well as positive links, between environmental factors and breast cancer risk. Where results are contradictory, we try briefly to address possible methodological issues that might help account for these differences. (lines 76-133).

• Beginning with the introductory framing section, and then continuing into each of the major subsections of the evidence portion of the report, we have added introductory and summary
paragraphs. The introductions raise major issues to be addressed and the summaries offer quick overviews of the previous concepts and/or data. The sections should help the reader consolidate the information, especially from the larger sections, and also provide a break in the more detailed text of the review.

- We have expanded our final concluding discussion to address specifically the strengths and limitations of the research models used to address potential connections between environmental exposures and risk for developing breast cancer.

- We have included one figure at the end of the section on framing concepts that situates the data we are about to present in a web-like model of interconnected factors, indicating the complexity of the biological, social, and lifestyle factors that ultimately mediate, and complicate, many of the possible links between environmental factors and breast cancer risk.

- We have included 5 tables, 4 of them fairly small and the other larger. In addition to breaking up the text, the tables provide information on the regulatory (IARC and NTP) classification for each of the exposures, as well as brief descriptions of major sources for each exposure.

More specific changes in response to the reviewer’s comments include:

- As suggested by the reviewer, we have changed the comment about the evidence to be presented (in both the abstract and the introduction) to the more neutral phrase, “The evidence on this topic is more extensive and of better quality than that previously available.”

- In the introduction (lines 54-58) we have clarified the phrase, “increasingly higher incidence of breast cancer over the past several decades”.

- In the abstract, we have clarified that the disease is breast cancer.

- We have changed the language in the introduction to indicate the correlation between increased use of chemicals in the decades following World War II, a time when parallel increases in breast cancer incidence was also observed. This change, followed by the addition of the organizational sentences and the methodology section, should make clearer our starting point for exploring the literature examining links, or lack thereof, between environmental factors and risk for breast cancer.

- We have removed the phrase “unacceptably high” from both the abstract and introduction and replaced it with more neutral language.

- We have included a paragraph that outlines the organization of the paper.
• In the summary at the end of the introductory section, we have replaced “these topics” with “these framing concepts”.

• We have added the missing decimal points in the confidence interval noted by the reviewer.

In addition, we have added several risk ratios, with their 95% confidence ranges, for studies where we had not previously offered that information.