

Author's response to reviews

Title: Air Pollution Attributable Postneonatal Infant Mortality in U.S. Metropolitan Areas

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Version: 2 Date: 17 Mar 2004

Manuscript ID: 2084538552278186

Submitted by: Reinhard Kaiser (RKaiser@cdc.gov)

Title: Air Pollution Attributable Postneonatal Infant Mortality in US Metropolitan Areas Journal: Environmental Health: A Global Access Science Source Type: Research
Other subject areas: Pediatrics, Pregnancy and childbirth Authors: Reinhard Kaiser, Isabelle Romieu, Sylvia Medina, Joel Schwartz, Michal Krzyzanowski and Nino Kunzli

Dear Editors-in-Chief,

Please find attached our revised manuscript 2084538552278186 for re-submission to Environmental Health. We have responded below point by point to the comments of the reviewers.

In response to the main comment of reviewer 1, we state now that our estimates are based on the best currently available information, leaving considerable uncertainty about the size of the true effect of particulate matter on infant mortality. Responding to major comments of reviewer 2, we estimated the expected number of annual deaths above exposure reference levels of 12.5 g/m³ and 7.5 g/m³ PM₁₀, and added alternative estimates of effects on infant and child mortality. However, we did not attempt to use non-US studies for a metaanalytic estimate because we believe that considerable differences in the quality of pollution (sources) and in the underlying susceptibility to infant deaths make the transfer of non-U.S. results to the U.S. a rather debatable undertaking. Similarities (or differences) in effect estimates across such studies do not resolve this inherent conflict, thus given the availability of U.S. results, we opt for using only this one for the quantification, and the remaining studies to discuss the issue of the evidence (qualitatively). For the same reasons we did not quantify the burden for other metropolitan areas. Finally, we added to the discussion about the plausibility of an air pollution effect on both SIDS and respiratory mortality and the likely mechanisms.

We modified the manuscript to be in accordance with the instructions for authors, including reformatting of the references.

Sincerely,

Dr. Reinhard Kaiser

Reviewer #1: C. Arden Pope, BYU

Major Comments:

1. This is an interesting paper that applies the results of the infant mortality and particulate pollution epidemiological study by Woodruff et al., and estimates attributable infant mortality in U.S. metropolitan areas due to particulate pollution. The basic approach has been used before for adult mortality, but this exercise has not previously been conducted and published for infant mortality.

2. Although I agree that air pollution related infant mortality is likely a public health problem, I do not think that it is wise to suggest that the estimates presented in the paper are "likely underestimates." There is a great deal of uncertainty about the size of the PM effect. These estimates are simply "reasonable estimates" based on very limited information.

Response: Modified as suggested.

Minor Comments:

1. Abstract and results. Is it 23 or 25 U.S. counties. A different number is given in the abstract and in the results.

Response: In abstract and methods we report 25 counties in 23 metropolitan areas.

2. Abstract. The U.S. is a country with low infant mortality rates, but also relatively low pollution levels.

Response: Modified as suggested.

3. The second paragraph of the Intro needs some editing.

Response: Edited as suggested.

4. Methods. Why were there so few metro areas that could be included in the analysis?

Response: The criteria for selection are stated in the methods section. Main criteria were a population of at least 500'000, and geographic distribution across the United States. We expect the results in the original study to be also driven by large areas (high data density). Given the influence of the background incidence rates on the burden assessment we consider our restriction on large areas appropriate, leading to more defensible numbers than the expansion to smaller areas. Thus, we greatly prefer not to change this methodological decision.

5. Dissuasion. There is not an adequate discussion about the assumptions made regarding the shape of the concentration response relationship.

Response: We expanded the discussion to acknowledge the shape of the function, including thresholds of effect.

6. Last paragraph. Please be specific about why the approach used in this analysis is a "prudent approach" and likely results in underestimating the PM effect.

Response: We agree that the terminology is ambiguous. We changed the respective sections to make clear that these are results based on a currently available "best estimate".

Level of interest: A paper whose findings are important to those with closely related research.

Quality of written English: The paper needs some editing for grammar, style, and consistency.

Response: We edited the text as suggested.

Comments

This is an important paper that quantifies the attributable risk of air pollution for infant mortality in 23 U.S. metropolitan areas. As such, it serves to provide a perspective on public health impacts on children from current exposures to air pollution versus other risk factors. The authors correctly apply the original epidemiologic study, current air pollution data and existing methodology for calculating health effects. Therefore, the quantitative conclusions are reasonable and scientifically plausible. There are several ways, however, in which the paper could be made even stronger and more defensible.

Major comment 1: It would be useful and perhaps more scientifically sound to rely on more than a single study as a basis for the estimates. The authors describe other studies that use different methodologies, that could serve as a basis for alternative estimates. These other studies include daily time-series analyses of air pollution and infant mortality, and cohort studies that relate prior air pollution to adverse birth outcomes such as low birth weight and premature births. These birth outcomes are known to impact overall survival rates. It would be of interest to calculate the attributable risk based on these studies.

Response: We added to discussion: We estimated the expected number of annual deaths above exposure reference level of 12.5 g/m³ and 7.5 g/m³ PM₁₀, and added alternative estimates of effects on infant and child mortality.

We reconsidered the use of non-US studies for a metaanalytic estimate but came back to our previous conclusion to restrict on the U.S. study. The main argument not to use non-US studies for a metaanalytic estimate is that the generalization to the US remains a target of criticism. It can be argued that the constituents (and thus the health relevance) of air pollution in the regions of these other studies are different, as are the background susceptibility (or rates) for infant mortality. Thus, the mere similarity in effect estimates could be a coincidence. We thus opt for the wider confidence intervals than what would result from a metaanalytic approach combining US and non-US studies. We profit from the availability of an U.S. study, thus, we believe that we do not need to add the uncertainty that is inherent in the geographic generalization usually required in regions without studies or on the global scale (e.g. Global Burden of Disease). As mentioned in the discussion, we also preferred not to derive survival rates and lost life expectancy given the considerable gap of knowledge to leap from death to time lost among infant deaths. We think this is a very important point and our paper discusses the arguments that lead our choice.

Major comment 2: The paper could be enhanced by applying the attributable risk to the base population to indicate the total magnitude of the effect, i.e., the expected number of deaths. Also, the authors should indicate whether it would then be reasonable to apply their estimate to all other metropolitan areas in the U.S. to obtain a full estimate of the impact.

Response: We welcome the suggestion to show the total magnitude and respective changes have been made. We estimated the expected number of annual deaths above exposure reference levels of 12.5 g/m³ and 7.5 g/m³ PM₁₀. Regarding the application to other areas, we have expanded our discussion on this issue. Given the variation in risks - as mentioned above - we abstain however from the quantification of the burden for other metropolitan areas.

Major comment 3: The authors should add some discussion about the plausibility of an air pollution effect on both SIDS and respiratory mortality and the likely mechanisms. Also, readers would benefit

from a discussion of the positive aspects and potential shortcomings of the Woodruff study.

Response: We expanded the discussion regarding air pollution effects on SIDS and respiratory mortality. We kept what was already mentioned in the discussion about positive aspects and potential shortcomings of the Woodruff study.

Minor comment 1: Page 3, para 2: It is incorrect that the burden of outdoor air pollution has never been applied to infant mortality. The paper cited by Ezzati et al. (2002) described an effort by WHO to determine, among other risk factors, the effects of air pollution on the global burden of disease. In doing so, the worldwide effects of air pollution as represented by PM_{2.5}, or particles less than 2.5 microns, on infant mortality are estimated. However, the effects on infants are not disaggregated in the paper, although age-specific estimates are provided for disability-adjusted-life-years or DALYs in the full WHO report (The World Health Report, 2002).

Response: We agree and modified the introduction accordingly.

Minor comment 2: page 5, para 1: misspelled "United" as "Unites"

Response: Modified as suggested.

Minor comment 3: page 5, para 1: would the final results have change if the total attributable risk was based on a population-weighting of the city-specific risks rather than averaging?

Response: We added to the discussion: The total attributable risk based on population-weighting was higher than averaging across counties (7%, 95% CI 4-12% vs. 6%, 95% CI 3-11%), indicating that lack of control for risk factors in the original study may have resulted in an underestimate of the total effect.

Minor comment 4: page 8, para 2: add "SWoodruff study, but have been shown.."

Response: Modified as suggested.

Minor comment 5; page 8, para 2: Limiting the analysis to infants without LBW would probably result in an underestimate of the total effect.

Response: We added to the discussion: In addition, excluding infants with LBW may have resulted in increased social class homogeneity because low social class is a determinant of LBW (Spencer, Bambang et al. 1999), probably adding to an underestimate of the total effect estimated in our study.

Minor comment 6, page 9, para 1: What is the evidence for other pollutants and for potential synergism?

Response: We added to the discussion as suggested: Because it is generally not possible to assign effects of ambient air pollution to specific single pollutants, we considered PM as a surrogate measure of a more complex mixture. Part of the association between mortality and PM may be explained by the correlation of PM with other ambient air pollutants, and the estimated mortality may not be exclusively attributed to PM₁₀. This uncertainty needs to be taken into account in the assessment of benefits of policies that target single pollutants rather than the mixture.

Level of interest

A paper of considerable general medical or scientific interest

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Philippe Grandjean, David Ozonoff

Editors-in-Chief

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