Author’s response to reviews

Title: Effects of Ambient Air Pollution on Functional Status in Patients with Chronic Congestive Heart Failure: A Repeated-Measures Study.

Authors:

Gregory A Wellenius (gwelleni@bidmc.harvard.edu)
Gloria Y Yeh (gyeh@bidmc.harvard.edu)
Brent A Coull (bcoull@hsph.harvard.edu)
Helen H Suh (hsuh@hsph.harvard.edu)
Russell S Phillips (rphillips@bidmc.harvard.edu)
Murray A Mittleman (mmittlem@bidmc.harvard.edu)

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Author’s response to reviews: see over
July 3, 2007

Editors-in-Chief, *Environmental Health*

Dear Dr. Grandjean and Dr. Ozonoff,

My colleagues and I are pleased to submit a revised version of our manuscript, “Effects of Ambient Air Pollution on Functional Status in Patients with Chronic Congestive Heart Failure: A Repeated-Measures Study” for consideration for publication in *Environmental Health*.

We thank both Reviewers for their time, interest, and thoughtful comments. We have revised the manuscript according to their suggestions and a point-by-point response is attached.

Thank you in advance for your continued consideration of this work. Please feel free to contact me by phone at 617-632-7680 or by email at gwelleni@bidmc.harvard.edu if I may be of any assistance.

Sincerely,

Gregory A. Wellenius, ScD
We thank both Reviewers for their time, interest, and thoughtful comments. We have revised the manuscript according to their suggestions and offer this point-by-point response.

**Reviewer 1**

**Comment:** Table 2: It is not clear whether this is the distribution over the study period or the distribution of the exposure assigned to the observations. The time period and location, as well as the number of observations should be presented.

**Response:** We thank the Reviewer for noting this deficit and have modified Table 2 as suggested. In addition, the text has been modified to indicate that the summary measures presented were obtained using the daily values over the entire study period (pg 7, lines 13 and 14).

**Comment:** Table 2 It may be helpful to also show how the air pollution concentrations varied within the individual. Since each subject was only observed over 3 months, air pollution contrasts may have been comparably low.

**Response:** The Reviewer raises an important point. The subject-specific range (max minus min PM2.5 value calculated for each patient) varied from 0.7 to 50.9 µg/m³ with a mean of 10.9 µg/m³ and a median of 8.0 µg/m³. Thus, although each participant was observed within a 3-month period, more than half of subjects exhibited considerable within-person variability in PM2.5 exposure values. A statement to this effect has been added to the Results (pg 7, lines 14-18).

**Comment:** Discussion: The analyses controlled for weather, measurement occasion, and treatment group but not for potential individual confounders that may have changed over time and coincided with air pollution changes. Wouldn’t it be possible that controlling for individual characteristics that changed over time may have helped to explain the variation of the BNP measurements and thereby improved the estimation of the air pollution effect?

**Response:** The Reviewer correctly notes that an additional limitation of this study is that we were not able to evaluate non-environmental sources of biologic variability such as changes in diet, health status, or medication usage. It is possible that accounting for these or other important time-varying factors would significantly reduce the apparent within-subject variability of BNP. A statement to this effect has been added to the Discussion (pg 11, lines 15-18).

**Reviewer 2**

**Comment:** It may be worthwhile noting that acute smoking (although not completely similar to PM exposure, but that shares many same mechanisms) can mediate diastolic function changes and in a congruent fashion perhaps repeated or serial echocardiography using newer software could be a viable alternative to show a PM-
induced effect on cardiac parameters capable of promoting CHF in certain at-risk people (e.g. hypertensives or elderly)

**Response:** We appreciate the Reviewer’s insightful suggestion and have added statements to this effect to the Discussion (top of pg 11).