Author's response to reviews

Title: Ambient pollutants, polymorphisms associated with microRNA processing and adhesion molecules: the Normative Aging Study

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Author's response to reviews: see over
Dear Drs. Ozonoff and Grandjean,

We appreciate the opportunity to publish in Environmental Health and have made the formatting changes below, which we hope will clarify the manuscript. No changes to the regarding the content of the research have been made.

Best,
Elissa Wilker

Note: All font changed to Times Roman

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Background

- 2 spaces added before start of sentence
  - “MicroRNA (miRNA) is thought to be involved in cardiovascular regulation”

Methods

- Comma added after black carbon:
  - Previous Version: […] matched to air pollution monitoring for fine particulate matter (PM$_{2.5}$) black carbon and sulfates.
  - New Version: for fine particulate matter (PM$_{2.5}$), black carbon, and sulfates (SO$_4^2$)

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- Reference about inflammation moved before redox signaling
  - Previous Version: is thought that miRNAs play a role in a number of pathogenic pathways including angiogenesis [26], inflammation, redox signaling [27, 28], and stress response [29].
  - New Version: It is thought that miRNAs play a role in a number of pathogenic pathways including angiogenesis [26], inflammation [27], redox signaling [28], and stress response [29].
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- sICAM and sVCAM measurements formatting problem and lengthy sentence (bottom of the page)
  - Previous Version: sICAM-1 and sVCAM-1 were measured in the serum during medical exam visits from 1999 through 2008 and were measured by an ELISA assay (R & D Systems, Minneapolis, MN), with a sensitivity of 0.35 ng/mL for sICAM-1 and 2.0 ng/mL for sVCAM-1.
  - New Version: sICAM-1 and sVCAM-1 were measured in the serum during medical exam visits from 1999 through 2008 by ELISA assay (R & D Systems, Minneapolis, MN), with a sensitivity of 0.35 ng/mL for sICAM-1 and 2.0 ng/mL for sVCAM-1.

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- Bottom line: A priori italicized \( \rightarrow \) \textit{a priori}. Now the term is italicized in both locations where it appears (also page 8 in statistical methods)
  - We used seven day moving averages as our \textit{a priori} time period of interest and also examined five and nine day

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- Top line: Season changed to “seasonality” to match description in tables
  - Previous Version: apparent temperature (a measure of perceived temperature) and season.
  - New Version: apparent temperature (a measure of perceived temperature) and seasonality using sine and cosine of month.

- Sentence about restricting to white race removed, since this is already described. The full NAS is 97% white. This population with icam/vcam and SNPs is 96% white. We remove this sentence to avoid any confusion about these percentages.
Results

- Added the word “analyses” before SO$_4^{2-}$ to clarify the intention of this sentence
  - Previous Version: Fewer visits were available for SO$_4^{2-}$ because these measures started later
  - New Version: Fewer visits were available for SO$_4^{2-}$ analyses because these measures started later and filters were missing on some days

- Added “%” for the IQR changes in SO$_4$ as well as mentioned that SO$_4$ 7 day average for VCAM did not meet statistical significance.
  - Previous Version: An IQR change in SO$_4$ 2- (1.39 µg/m$^3$) was associated with 1.4 (95%CI: 0.04, 2.7) higher sICAM-1 levels, and 1.6 (95%CI: -0.41,3.7) higher sVCAM-1.
  - New Version: An IQR change in SO$_4^{2-}$ (1.39 µg/m$^3$) was associated with 1.4% (95%CI: 0.04, 2.7) higher sICAM-1 levels, and a non-statistically significant change of 1.6% (95%CI: -0.41,3.7) higher sVCAM-1.

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- Line 2: Changed SNP effects to SNP associations
  - Previous Version: we restricted our analysis of SNP effects and their interactions to models with PM$_{2.5}$
  - New Version: Because BC was not significantly associated with sICAM-1 or sVCAM-1, and SO$_4^{2-}$ was missing for a large number of days in addition to being strongly correlated with PM$_{2.5}$, we restricted our analysis of SNP associations and their interactions to models with PM$_{2.5}$.

- Paragraph 2: Created a new paragraph to describe the Main Effects analysis (as opposed to having it included with the interactions).

- End of Paragraph 2: .4 should be .04 as in the table.
  - p=0.03 and 0.04
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- The description of the “marginally significant results for SO4 changed to not be rounded up so it matches the table.

**Previous Version:** We observed significant associations for sICAM-1 in our models of seven day moving averages for both PM$_{2.5}$ and marginally significant ($p=0.05$) results for SO$_4^{2-}$.

  - We observed significant associations for sICAM-1 in our models of seven day moving averages for both PM$_{2.5}$ and marginally significant ($p=0.044$) results for SO$_4^{2-}$.

Table 2:

Added parentheses surrounding 95% CIs.