Supplemental Material

Environmental Cadmium and Lead Exposures and Hearing Loss in US Adults: the National Health and Nutrition Examination Survey, 1999 to 2004

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<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participants (N=3698)</th>
<th>Non-Participants (N=1565)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupation noise exposure (O*NET score)</td>
<td>3.06 (± 0.02)</td>
<td>3.12 (± 0.02)</td>
<td>0.052</td>
</tr>
<tr>
<td>Age (y)</td>
<td>42.06 (± 0.28)</td>
<td>42.09 (± 0.43)</td>
<td>0.956</td>
</tr>
<tr>
<td>Body mass index (wtkg/htm)</td>
<td>28.04 (± 0.15)</td>
<td>28.47 (± 0.31)</td>
<td>0.212</td>
</tr>
<tr>
<td>PTA Hearing Thresholds (dB)</td>
<td>12.78 (± 0.24)</td>
<td>16.95 (± 0.40)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hearing Loss (PTA&gt;25dB, %)</td>
<td>11.9</td>
<td>28.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Noise notch (%):</td>
<td>17.7</td>
<td>17.0</td>
<td>0.592</td>
</tr>
<tr>
<td>Sex (Male %)</td>
<td>48.6</td>
<td>50.3</td>
<td>0.275</td>
</tr>
<tr>
<td>Race ethnicity (%)</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>72.5</td>
<td>65.7</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>10.5</td>
<td>11.1</td>
<td></td>
</tr>
<tr>
<td>Mexican American</td>
<td>6.6</td>
<td>9.3</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>10.4</td>
<td>13.9</td>
<td></td>
</tr>
<tr>
<td>Education (%)</td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&lt; High School</td>
<td>16.6</td>
<td>21.8</td>
<td></td>
</tr>
<tr>
<td>High School</td>
<td>25.1</td>
<td>24.5</td>
<td></td>
</tr>
<tr>
<td>&gt; High School</td>
<td>58.3</td>
<td>53.7</td>
<td></td>
</tr>
<tr>
<td>Ototoxic medication (Current use %)</td>
<td>15.9</td>
<td>14.8</td>
<td></td>
</tr>
<tr>
<td>Cumulative cigarette pack-years (%)</td>
<td></td>
<td></td>
<td>0.273</td>
</tr>
<tr>
<td>Never</td>
<td>53.7</td>
<td>54.3</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>33.7</td>
<td>31.3</td>
<td></td>
</tr>
<tr>
<td>≥20</td>
<td>12.5</td>
<td>14.4</td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>23.2</td>
<td>24.8</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>4.1</td>
<td>6.4</td>
<td></td>
</tr>
<tr>
<td>Firearm noise exposure (Exposed %)</td>
<td>7.5</td>
<td>9.2</td>
<td></td>
</tr>
<tr>
<td>Recreation noise exposure (Exposed %)</td>
<td>26.0</td>
<td>28.5</td>
<td></td>
</tr>
</tbody>
</table>

Continuous variables: survey t-test, age-adjusted
Categorical variables: 2*2 table or 2*C table : survey X_square (Rao-Scott Chi-Square Test)

Subjects (N=5263) are eligible for the audiometric data
Participants (N=3698) are the individuals having all interest variables in this study: hearing thresholds, hearing loss, age, BMI, sex, race ethnicity, ototoxic medication, cumulative cigarette packyears, hypertension, diabetes mellitus, occupational noise score, and firearm and recreation noise exposure
Occupation noise (1 < O*NET noise scale < 5)
PTA at speech frequencies (Pure tone means at 0.5, 1, 2, 4 KHz)
Hearing loss was defined as PTA at speech frequencies > 25 dB
Noise Notch (Hearing threshold at 3, 4, and/or 6 kHz is at least 10 dB greater than at 1 or 2 kHz and at least 10 dB greater than at 6 or 8 kHz.)

Non-Participants (N=1137, 1492, 1563, 1559, 1119, 1343, 1563, 1560, 1557, and 1565 for the others) are the individuals having the variable to be compared
### Supplemental Material, Table S2. Participant characteristics by hearing loss status (N=3698a).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All participants (N=3698)</th>
<th>Not Hearing Loss (N=3257)</th>
<th>Hearing Loss (N=441)</th>
<th>P-valueb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Lead (ug/dL)</td>
<td>1.94 (±0.04)</td>
<td>1.91 (±0.04)</td>
<td>2.17 (±0.09)</td>
<td>0.006</td>
</tr>
<tr>
<td>Blood Cadmium (ug/L)</td>
<td>0.56 (±0.01)</td>
<td>0.55 (±0.01)</td>
<td>0.67 (±0.04)</td>
<td>0.003</td>
</tr>
<tr>
<td>Age (y)</td>
<td>42.06 (±0.28)</td>
<td>40.45 (±0.29)</td>
<td>54.81 (±0.66)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Body mass index (wtkg/htm)</td>
<td>28.04 (±0.15)</td>
<td>28.03 (±0.15)</td>
<td>28.06 (±0.36)</td>
<td>0.941</td>
</tr>
<tr>
<td>Pure tone average hearing thresholds (dB)c</td>
<td>12.78 (±0.24)</td>
<td>10.98 (±0.16)</td>
<td>27.03 (±0.68)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Occupation noise exposure (O*NET score)d</td>
<td>3.06 (±0.02)</td>
<td>3.04 (±0.02)</td>
<td>3.25 (±0.04)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sex (Male %)</td>
<td>48.6</td>
<td>46.4</td>
<td>66.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Race ethnicity (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>72.5</td>
<td>71.5</td>
<td>80.6</td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>10.5</td>
<td>11.2</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>Mexican American</td>
<td>6.6</td>
<td>7.1</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>10.4</td>
<td>10.2</td>
<td>11.5</td>
<td></td>
</tr>
<tr>
<td>Education (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>&lt; High School</td>
<td>16.6</td>
<td>15.1</td>
<td>28.3</td>
<td></td>
</tr>
<tr>
<td>High School</td>
<td>25.1</td>
<td>24.7</td>
<td>28.2</td>
<td></td>
</tr>
<tr>
<td>&gt; High School</td>
<td>58.3</td>
<td>60.2</td>
<td>43.4</td>
<td></td>
</tr>
<tr>
<td>Ototoxic medication (Current use %)</td>
<td>15.9</td>
<td>14.8</td>
<td>24.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Cumulative cigarette pack-years (%)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Never</td>
<td>53.7</td>
<td>55.4</td>
<td>40.8</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>33.7</td>
<td>34.6</td>
<td>27.3</td>
<td></td>
</tr>
<tr>
<td>≥20</td>
<td>12.5</td>
<td>10.1</td>
<td>31.9</td>
<td></td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>23.2</td>
<td>20.6</td>
<td>43.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>4.1</td>
<td>3.2</td>
<td>11.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Firearm noise exposure (Exposed %)</td>
<td>7.5</td>
<td>6.8</td>
<td>13.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Recreation noise exposure (Exposed %)</td>
<td>26.0</td>
<td>25.6</td>
<td>29.3</td>
<td>0.203</td>
</tr>
</tbody>
</table>

aHearing loss was defined as pure tone average at speech frequencies > 25 dB.
bSurvey t-test (age-adjusted) for continuous variables and survey (Rao-Scott) Chi-square test for categorical variables were used.
cPure tone average at speech frequencies at 0.5, 1, 2, and 4 kHz.
dOccupation noise (1 < O*NET noise scale < 5).
### Supplemental Material, Table S3. Percent change (95% CIs) of hearing thresholds (dB) by contribution of different variables in a multiple linear regression

<table>
<thead>
<tr>
<th>Variables</th>
<th>No.</th>
<th>Regression model&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cadmium Quintile (µg/L)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quintile 1 (0.10-0.20)</td>
<td>1013</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Quintile 2 (0.30-0.30)</td>
<td>553</td>
<td>-1.22 (-8.86, 7.07)</td>
</tr>
<tr>
<td>Quintile 3 (0.40-0.40)</td>
<td>581</td>
<td>1.68 (-5.60, 9.53)</td>
</tr>
<tr>
<td>Quintile 4 (0.50-0.70)</td>
<td>785</td>
<td>6.69 (-1.48, 15.53)</td>
</tr>
<tr>
<td>Quintile 5 (0.80-8.50)</td>
<td>690</td>
<td>13.78 (4.55, 23.82)</td>
</tr>
<tr>
<td><strong>Lead Quintile (µg/dL)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quintile 1 (0.20-0.80)</td>
<td>629</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Quintile 2 (0.90-1.30)</td>
<td>842</td>
<td>-0.5 (-9.94, 9.93)</td>
</tr>
<tr>
<td>Quintile 3 (1.40-1.80)</td>
<td>679</td>
<td>6.51 (-3.76, 17.89)</td>
</tr>
<tr>
<td>Quintile 4 (1.90-2.70)</td>
<td>734</td>
<td>10.22 (-0.40, 21.97)</td>
</tr>
<tr>
<td>Quintile 5 (2.80-54.00)</td>
<td>738</td>
<td>18.63 (7.35, 31.09)</td>
</tr>
<tr>
<td><strong>O*NET Noise at longest job (unit score change)</strong></td>
<td></td>
<td>7.15 (1.48, 13.13)</td>
</tr>
<tr>
<td><strong>Age (unit year change)</strong></td>
<td>6</td>
<td>1.38 (0.05, 2.73)</td>
</tr>
<tr>
<td><strong>Age&lt;sup&gt;2&lt;/sup&gt; (unit year change)</strong></td>
<td>6</td>
<td>0.01 (0.00, 0.03)</td>
</tr>
<tr>
<td><strong>Body mass index (10 wtkg/htm change)</strong></td>
<td></td>
<td>1.23 (0.85, 1.61)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1729</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Female</td>
<td>1969</td>
<td>-18.35 (-22.54, -13.94)</td>
</tr>
<tr>
<td><strong>Race ethnics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>1827</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>750</td>
<td>-11.88 (-17.96, -5.36)</td>
</tr>
<tr>
<td>Mexican American</td>
<td>805</td>
<td>-6.20 (-14.25, 2.60)</td>
</tr>
<tr>
<td>Other</td>
<td>316</td>
<td>0.78 (-8.49, 11.00)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
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<td></td>
</tr>
<tr>
<td>&lt; High School</td>
<td>974</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>High School</td>
<td>849</td>
<td>-9.78 (-16.99, -1.95)</td>
</tr>
<tr>
<td>&gt; High School</td>
<td>1875</td>
<td>-19.81 (-24.20, -15.16)</td>
</tr>
<tr>
<td><strong>Ototoxic medication</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3132</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Yes</td>
<td>566</td>
<td>2.53 (-4.88, 10.52)</td>
</tr>
<tr>
<td><strong>Cumulative cigarette packyears</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>2105</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>&lt;20</td>
<td>1183</td>
<td>-1.80 (-8.96, 5.92)</td>
</tr>
<tr>
<td>≥20</td>
<td>410</td>
<td>4.46 (-4.45, 14.30)</td>
</tr>
<tr>
<td><strong>Current dx of hypertension</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2713</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Yes</td>
<td>985</td>
<td>-1.01 (-5.92, 4.16)</td>
</tr>
<tr>
<td><strong>Current dx of diabetes mellitus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3485</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Yes</td>
<td>213</td>
<td>19.87 (8.93, 31.91)</td>
</tr>
<tr>
<td><strong>Noise Exposure at firearm</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3468</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Yes</td>
<td>230</td>
<td>10.19 (-0.52, 22.05)</td>
</tr>
<tr>
<td><strong>Noise Exposure at recreation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2844</td>
<td>0 (Reference)</td>
</tr>
<tr>
<td>Yes</td>
<td>854</td>
<td>3.43 (-4.01, 11.46)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Regression model was adjusted for age, age<sup>2</sup>, bmi, sex, race/ethnicity, ototoxic medication, cumulative cigarette packyears, current dx of hypertension, current dx of diabetes, and ocupation, recreation, and firearm noise. Cadmium models were further adjusted for lead; lead models were further adjusted for cadmium.
Supplemental Material, Figure S1. Graphical distribution of blood cadmium and lead with log-transformed hearing thresholds at speech frequencies (the average of thresholds at 0.5, 1, 2, and 4 kHz)

(a) Association with Cd(µg/L) levels

(b) Association with log-Cd(µg/L) levels

(c) Association with Pb(µg/dL) levels

(d) Association with log-Pb(µg/dL) levels

Smoothing models were adjusted for age, age², body mass index, sex, race/ethnicity, education, ototoxic medication, cumulative cigarette pack-years, hypertension, diabetes, occupation noise, recreation noise, firearm noise (d.f.=4, 3 for Cd, Pb; 5, 4 for log-Cd, log-Pb). Cadmium models were further adjusted for lead; lead models were further adjusted for cadmium.
Supplemental Material, Figure S2. Percent change (%) of hearing thresholds (dB) by blood cadmium and lead quintiles at each frequency from 0.5 kHz to 8 kHz

(a) 0.5 kHz

(b) 1 kHz

(c) 2 kHz

(d) 3 kHz

Blood Cadmium Quintiles

Blood Lead Quintiles

P-Trend=0.870

P-Trend=0.238

P-Trend=0.073

P-Trend=0.043

P-Trend=0.136

P-Trend=0.641

P-Trend=0.198

P-Trend=0.259
Regression models were adjusted for age, age^2, body mass index, sex, race/ethnicity, education, ototoxic medication, cumulative cigarette pack-years, hypertension, diabetes, occupation noise, recreation noise, firearm noise. Cadmium models were further adjusted for lead; lead models were further adjusted for cadmium.