Traffic-related air pollution exposures and risk of atrial fibrillation in the WHI

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Background

- Atrial fibrillation is the most common heart rhythm disorder
  - In the US: 5.1 million currently have AF; 12.1 million expected by 2050
  - Globally: 33.5 million currently have AF
- Established risk factors only explain 50-60% of cases
- Short-term pollution exposures have been associated with incidence and triggering
- Less is known about long-term exposure impacts

Image: Mayo Clinic
Determine the association of long-term exposures to air pollution on risk of incident AF in a large cohort of women

- Explore more pollutants than previous studies
- Explore non-linearity
- Determine susceptible subpopulations (if any)
Methods: Study Population

- Women’s Health Initiative (WHI)
  - 93,676 in OS; 68,132 in RCTs
  - Enrolled from 40 US clinical centers
  - Postmenopausal women 50-79
  - Baseline questionnaire, clinical measures
  - Followed up via questionnaires

- For the current analysis
  - No history of AF or no AF on baseline electrocardiogram
  - Were never enrolled in Medicare or Medicaid
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Methods: AF Ascertainment

- At least a single ICD-9 diagnosis code of 427.31 from inpatient, outpatient, or physician diagnosis while the subject was enrolled in the FFS within CMS
  - In a validation study, 98% of women with AF identified with an ECG or hospital records were identified by CMS linkage
  - Sensitivity analyses with women with at least two reports
Methods: Exposure Assessment

- All residential addresses (baseline and follow-up) geocoded
- Time-varying annual average exposures assigned at each address
  - University of Washington spatio-temporal models
    - $\text{PM}_{10}$
    - $\text{PM}_{2.5}$
    - $\text{NO}_2$
    - $\text{SO}_2$
  - Distance to major roadways
    - US Census Feature Classes A1-A3

Sampson PD et al. Atmos Environ 2013
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Sampson PD et al. Atmos Environ 2013
Methods: Statistical Methods

- Time-varying Cox proportional hazards models
- Deviations from linearity assessed with penalized splines
  - When deviations existed, use quartiles to model dose-response

- All models adjusted for
  - Study component (OS or RCT)
  - Demographics (age, race/ethnicity)
  - AF risk factors (BMI, HRT use, smoking status and pack-years, systolic and diastolic blood pressure, educational attainment, household income, physical activity, overall diet quality, and alcohol consumption)

- Assessed effect modification by
  - Age
  - Smoking status
  - Comorbidities
  - Individual SES (educational attainment, family income)
  - Region
Cohort Characteristics

- 87% white
- Most were current (43%) or former (23%) HRT users
- Most (52%) were never smokers
  - Among smokers, women had smoked 10.2 pack-years on average
- Average BMI: 27.9 kg/m²
- 41% had a college education or more
- 20% had a family income above $75,000
- At baseline, few had existing comorbidities
  - 4.2% with diabetes; 14.2 with high cholesterol
## Distributions of the Exposures

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Median</th>
<th>25th Percentile</th>
<th>75th Percentile</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PM$_{10}$ (µg/m$^3$)</strong></td>
<td>20.7</td>
<td>5.0</td>
<td>20.3</td>
<td>17.5</td>
<td>23.4</td>
<td>1.1</td>
<td>80.7</td>
</tr>
<tr>
<td><strong>PM$_{2.5}$ (µg/m$^3$)</strong></td>
<td>11.5</td>
<td>2.9</td>
<td>11.3</td>
<td>9.5</td>
<td>13.4</td>
<td>1.7</td>
<td>25.6</td>
</tr>
<tr>
<td><strong>NO$_2$ (ppb)</strong></td>
<td>12.3</td>
<td>6.0</td>
<td>11.2</td>
<td>7.5</td>
<td>16.0</td>
<td>0.5</td>
<td>45.6</td>
</tr>
<tr>
<td><strong>SO$_2$ (ppb)</strong></td>
<td>1.9</td>
<td>0.3</td>
<td>1.9</td>
<td>1.7</td>
<td>2.1</td>
<td>0.9</td>
<td>2.6</td>
</tr>
</tbody>
</table>

### Distance to the nearest (m)

<table>
<thead>
<tr>
<th></th>
<th>Distance to the nearest (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A1</strong></td>
<td>4,285.8</td>
</tr>
<tr>
<td><strong>A2</strong></td>
<td>4,020.0</td>
</tr>
<tr>
<td><strong>A3</strong></td>
<td>536.0</td>
</tr>
</tbody>
</table>
Pollutant Exposures and Risk of AF

- Hazard Ratio (95% CI)
  - PM<sub>10</sub>
  - PM<sub>2.5</sub>
  - SO<sub>2</sub>
  - NO<sub>2</sub>
Distance to Road and Risk of AF

Harzard Ratio (95% CI)

- **Basic**
- **Multivariable**
No consistent evidence of effect modification with PM$_{10}$ or PM$_{2.5}$

No evidence of effect modification for NO$_2$ or distance to road
Strengths and Limitations

- Nationwide prospective study
- Wide exposure distributions
  - Full distributions of some pollutants below current USEPA standards
- Extensive follow-up
- Multiple exposures with high spatial and temporal resolution

- Exposures estimated only at the home address
- Potential for missed AF cases
  - Between enrollment in the cohort and enrollment in CMS
  - Asymptomatic cases
- Cohort is all female and postmenopausal, mostly white
  - May limit generalizability
Conclusions

- Among this cohort of postmenopausal women, traffic related exposures (NO\textsubscript{2}, distance to A1 roadways) were associated with an increased risk of incident AF

- No clear susceptible subpopulations
Chancellor Hohensee
Isabel Holland
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WHI

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Questions?
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