Long-term air pollution exposure and incident dementia in American elderly population

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Dementia is a major public health challenge with substantial economic and social burden. The most common type of dementia is Alzheimer’s disease.

The National Alzheimer’s Project (NAPA) was signed in law, and the National Plan to address Alzheimer's disease and related dementias (ADRD) was launched.

Efforts to identify and intervene on modifiable factors that prevent or delay the onset of dementia are critical to combating the dementia epidemic (national priority).

Source: United National Population Database and Age Wave calculation
Aging and genetic risk factors do not fully explain the cause of ADRD and PD. Growing evidence indicates that **AIR POLLUTION** could be implicated in the risk, development and progression of brain disease.

Air pollution is highly prevalent and modifiable by public policy with benefits at the population level.
**Objective:** To investigate the association between long-term exposure to air pollution and incident dementia in American elderly population

**EXPOSURE**
- High resolution (daily, 1km) ground-level PM$_{2.5}$, NO$_2$, and ozone from ensemble-learning

**HEALTH**
- Individual-level Medicare health records from 2000-2018

**METHODS**
- Statistical methods (survival analysis) to look at chronic effects of air pollution
Air Pollution exposure assessment (PM$_{2.5}$, NO$_2$, O$_3$)

Annual mean PM$_{2.5}$ and NO$_2$ (2000-2016), warm-season mean O$_3$ (2000-2016, May-Oct)

5-year moving averages

**Monitoring Data**
- Meteorology
- Satellite data
- Land use terms
- CTM outputs
- Other data

**Ensemble**
- Neural Network
- Random Forest
- Gradient Boosting

Source: Di et al. (2019a, 2019b); Requia et al. (2020)
Study population

Medicare population aged 65+ who were always (2000-2018) enrolled in

1. Medicare fee-for-service (FFS) program
2. Both Part A (hospital insurance) and Part B (medical insurance)
3. 5-year “clean” period (dementia free)

To really capture the 1st diagnosis of ADRD, and better approximate incidence
Medicare Chronic Conditions Warehouse (CCW database):

Includes pre-defined indicators for all-cause dementia and Alzheimer’s disease (AD); based on Medicare inpatient and outpatient claims, Carrier claims (primarily doctor visits), skilled nursing facility, and home health-care claims.

1st cohort (dementia)
Followed until first diagnosis of dementia, or death, or end of study.
2 million dementia cases out of 12.2 million subjects

2nd cohort (AD)
Followed until first diagnosis of AD, or death, or end of study.
0.8 million AD cases out of 12.5 million subjects

Outcome assessment
Cox proportional hazard model (survival analysis)

- Fit single-, bi-, and tri-pollutant Cox proportional hazard models:
  - used GEE (generalized estimating equation) to account for spatial dependence

- Exposure to air pollution included as a time-varying variable:
  - For each year of follow-up, we estimated a **5-year moving average** of the past exposure to each pollutant (annual PM$_{2.5}$, annual NO$_2$, and warm-season O$_3$) for each participant.

- Baseline hazard: stratify on individual characteristics (sex, race, Medicaid eligibility, and age at study entry)

- Neighborhood-level SES (% Hispanic, % Black, median household income, median home value, % below poverty level, % owner-occupied housing, % of not graduating high school)

- Behavioural risk factors (BMI, smoking)

- Healthcare capacity (# of hospitals, MD))

- Residual confounding by spatial/temporal trends (region, calendar years)
PM$_{2.5}$ and NO$_2$ are associated with incident dementia and AD

- PM$_{2.5}$ and NO$_2$ were significantly associated with incident dementia and AD.

- While hazard ratios for warm-season O$_3$ were not elevated

\textit{Shi et al., Nature Communications (2021)}
Concentration-response (C-R) relationships

Shi et al., Nature Communications (2021)
Black, lower SES, urban residents are at higher risks

Black, Medicaid-eligible (i.e. lower SES), urban residents are particularly vulnerable

Shi et al., Nature Communications (2021)
Sensitivity analysis

- 10-year “clean” period (dementia free)

- Alternative exposure time window (lags 10, 5, 1, or 0)
  - Shorter time windows between exposure and disease showed higher effect estimates - implying an acceleration of an existing process (i.e., accelerating cognitive decline which was already well developed).

- Adjusting for comorbidities (diabetes, hypertension, stroke, and heart failure)

- Assessing the effect of possible outcome misclassification (assuming non-differential)
  - Suggest that misclassification has somewhat biased our findings to the null
    - Fit linear regression models for the rate of dementia or AD (events/person-time)
    - Used sensitivity and specificity for the outcome classification from Taylor et al (2009), and adjusted the observed case counts for each zip code in the stratified Poisson model
A national cohort study (2000–2018) of long-term air pollution exposure and incident dementia in older adults in the United States


Dr. Kyle Steenland
Identified more AD/dementia cases vs Inpatient claims only

Long-term effects of PM$_{2.5}$ on neurological disorders in the American Medicare population: a longitudinal cohort study

Lihua Shi*, Xiao Wu*, Mahdieh Danesh Yazdi, Danielle Braun, Yara Abu Awad, Yaguang Wei, Pengfei Liu, Qian Di, Yun Wang, Joel Schwartz, Francesca Dominici, Marianthi-Anna Kroumourtzoglou†, Antonella Zanobetti†

<table>
<thead>
<tr>
<th></th>
<th>AD</th>
<th>Dementia</th>
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<tbody>
<tr>
<td>Current study using Medicare CCW database (2000-2016)</td>
<td>5,646,187</td>
<td>11,121,272</td>
</tr>
<tr>
<td>Number of admissions</td>
<td>403,149,214</td>
<td>379,921,997</td>
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<tr>
<td>Total person-years</td>
<td></td>
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<tr>
<td>Previous study* using Medicare inpatient claims (2000-2016)</td>
<td>2,490,431</td>
<td>1,233,132</td>
</tr>
<tr>
<td>Number of admissions</td>
<td>475,820,277</td>
<td>478,636,053</td>
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<tr>
<td>Total person-years</td>
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To allow for a fair comparison, we used the same inclusion/exclusion criteria and restricted to the same time period and geographic region:

Dementia 11 million vs 1 million
AD 5.6 million vs 2.5 million

Hospitalization records only, would miss a lot of dementia cases!
Next move

- Whether there is a causal link between PM$_{2.5}$, NO$_2$, and AD/dementia?

- Which PM$_{2.5}$ components are critical for brain health? Important for policy making.

\textit{Preliminary results}

![Graph showing preliminary results of PM$_{2.5}$ and its components on dementia hazard ratio.](image-url)
Questions?

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