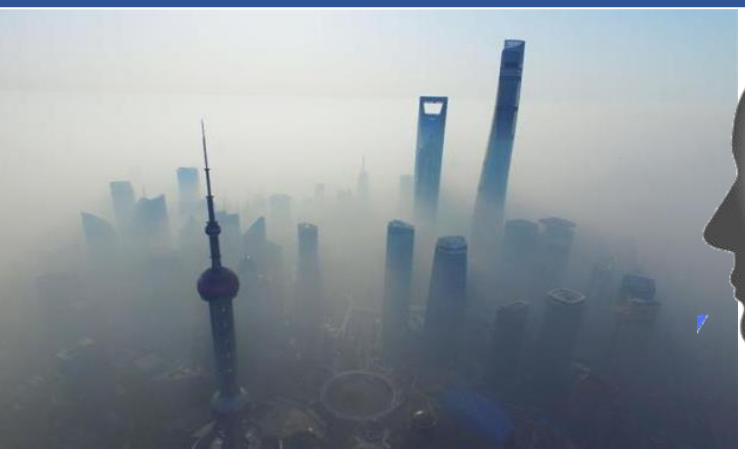
Long-term air pollution exposure and incident dementia in American elderly population



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Emory BrainTalk Live, Sept 13, 2022

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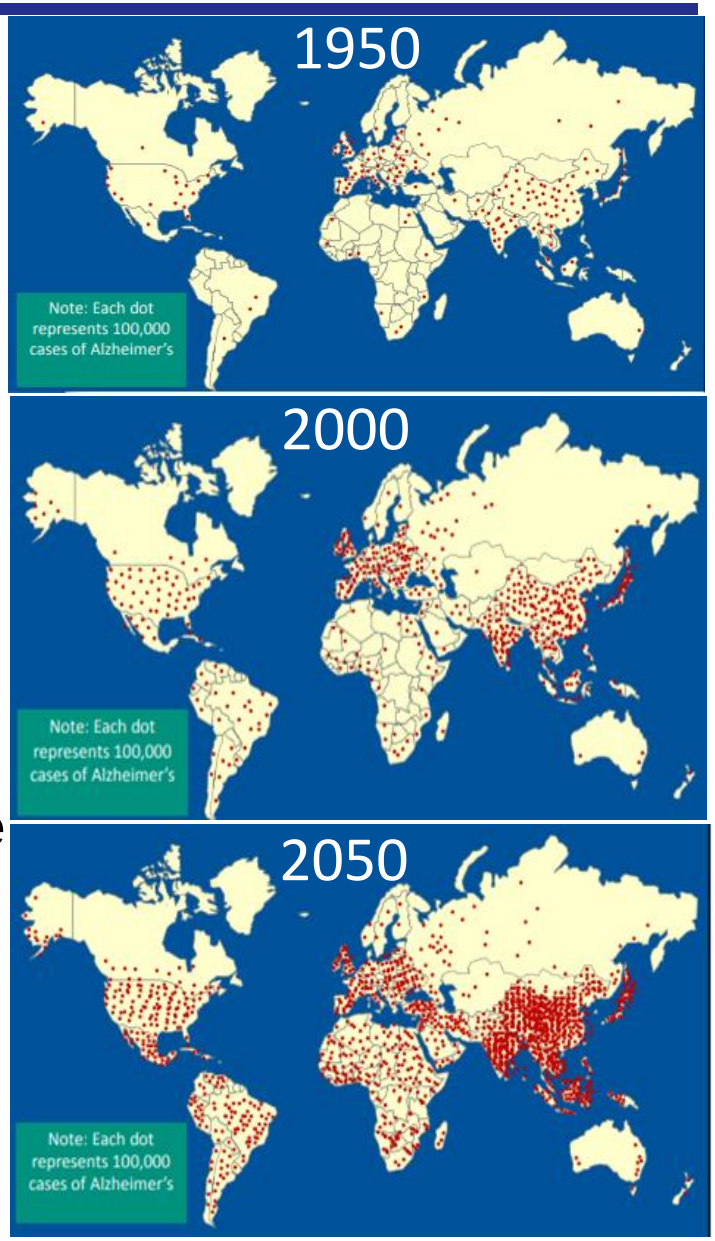
Dementia as a public health priority

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

50 million now | **152** million by 2050

- 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).



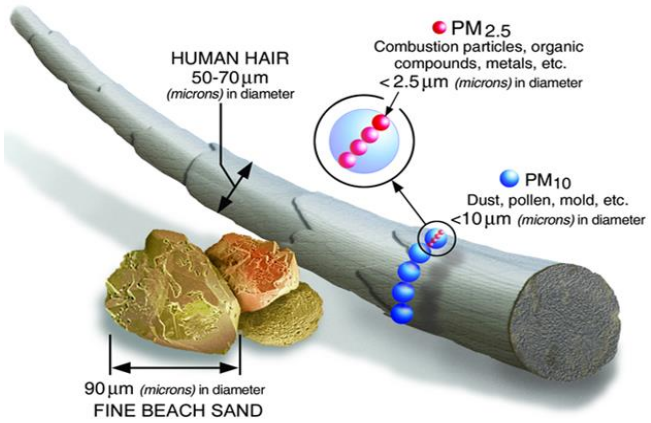
Source: United National Population Database and Age Wave calculation

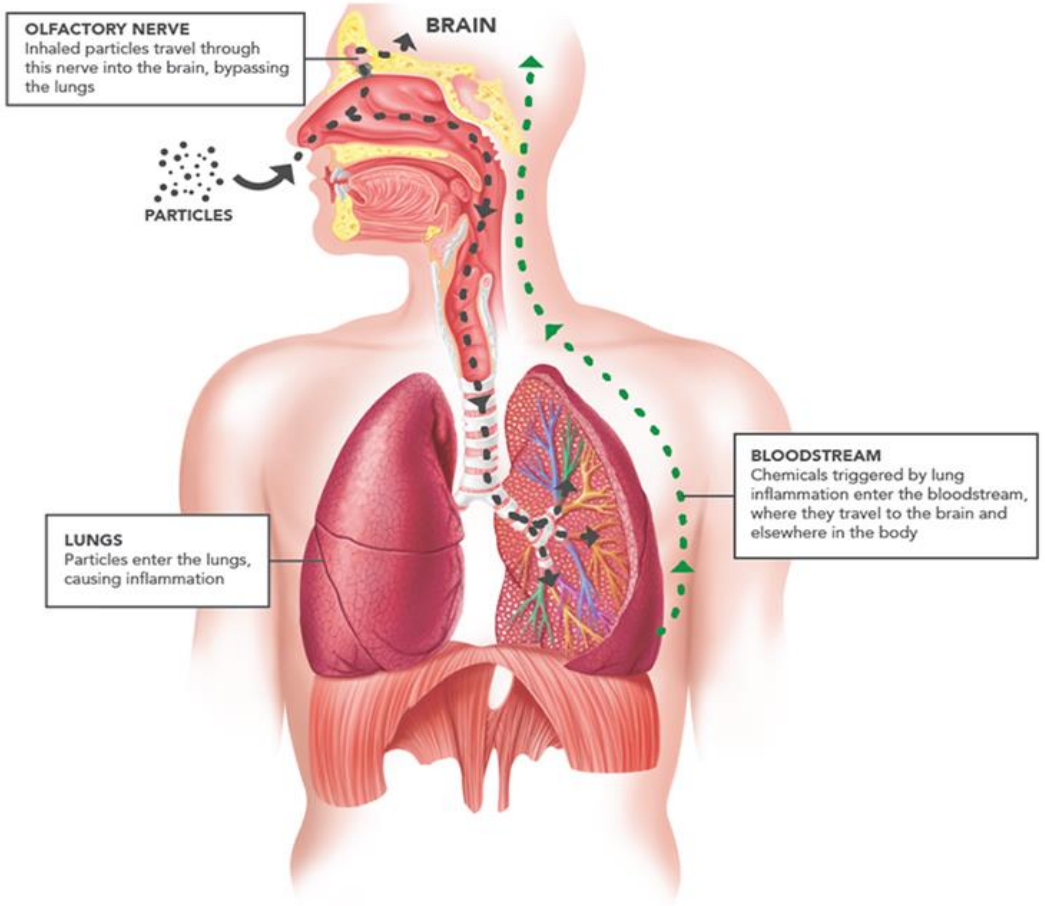
Air pollution might be an important risk factor

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.

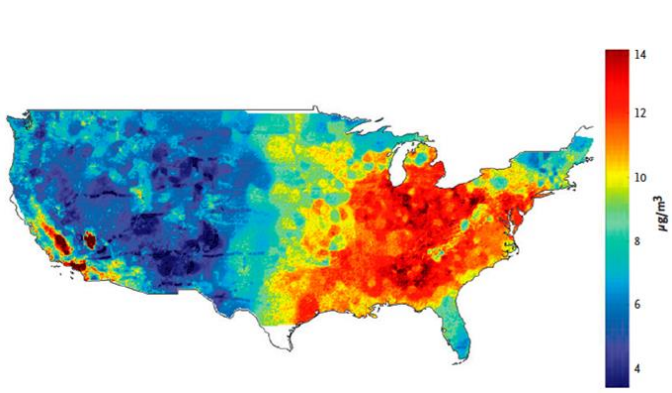
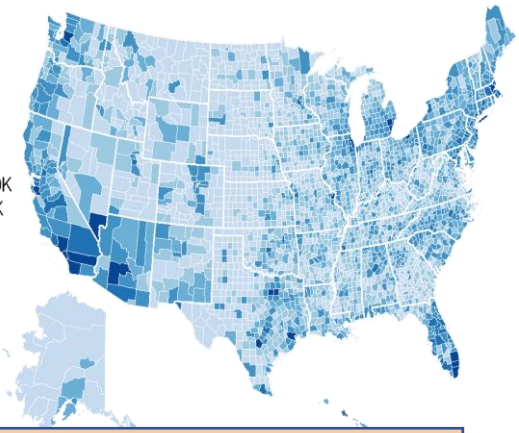
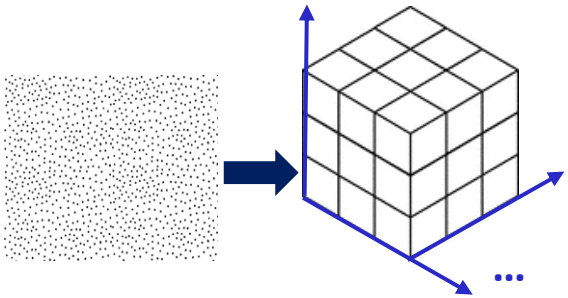
Air pollution is highly prevalent and modifiable by public policy with benefits at the population level.





A nationwide study

Objective: To investigate the association between long-term exposure to air pollution and incident dementia in American elderly population

EXPOSURE	HEALTH	METHODS
		
High resolution (daily, 1km) ground-level $PM_{2.5}$, $NO_{2,}$ and ozone from ensemble-learning	Individual-level Medicare health records from 2000-2018	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

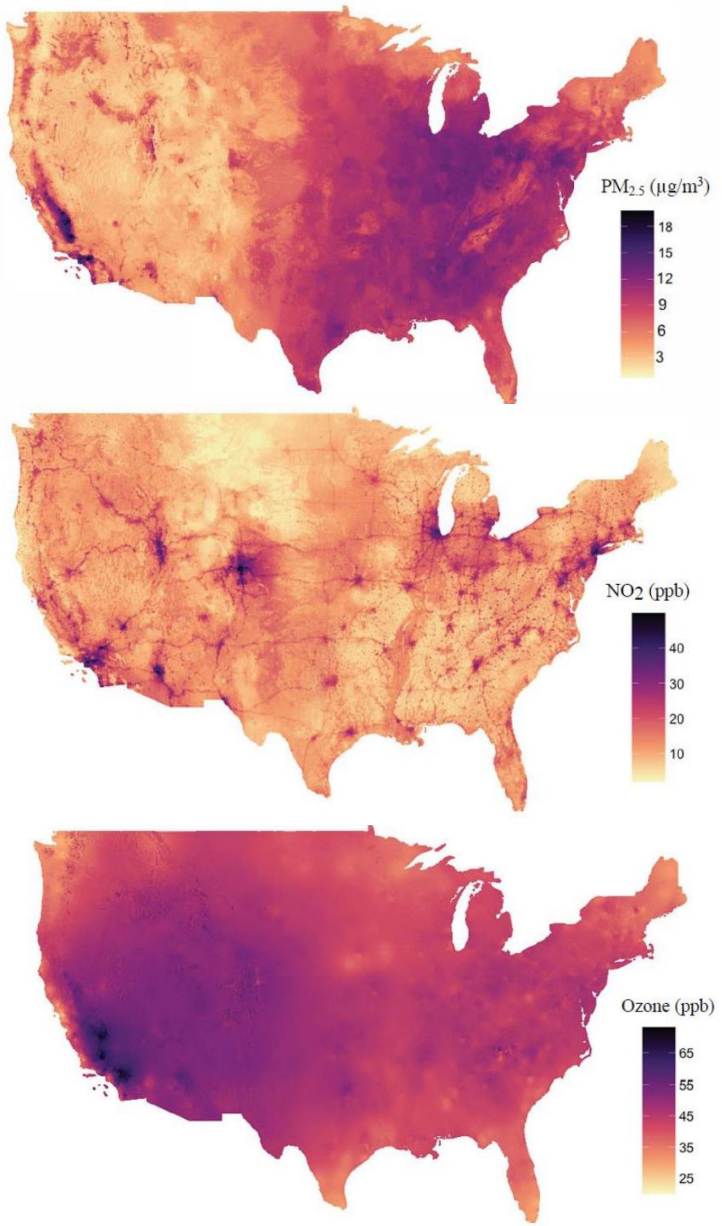
Monitoring Data

- Meteorology
- Satellite data
- Land use terms
- CTM outputs
- Other data

↓

Ensemble

Neural Network
Random Forest
Gradient Boosting



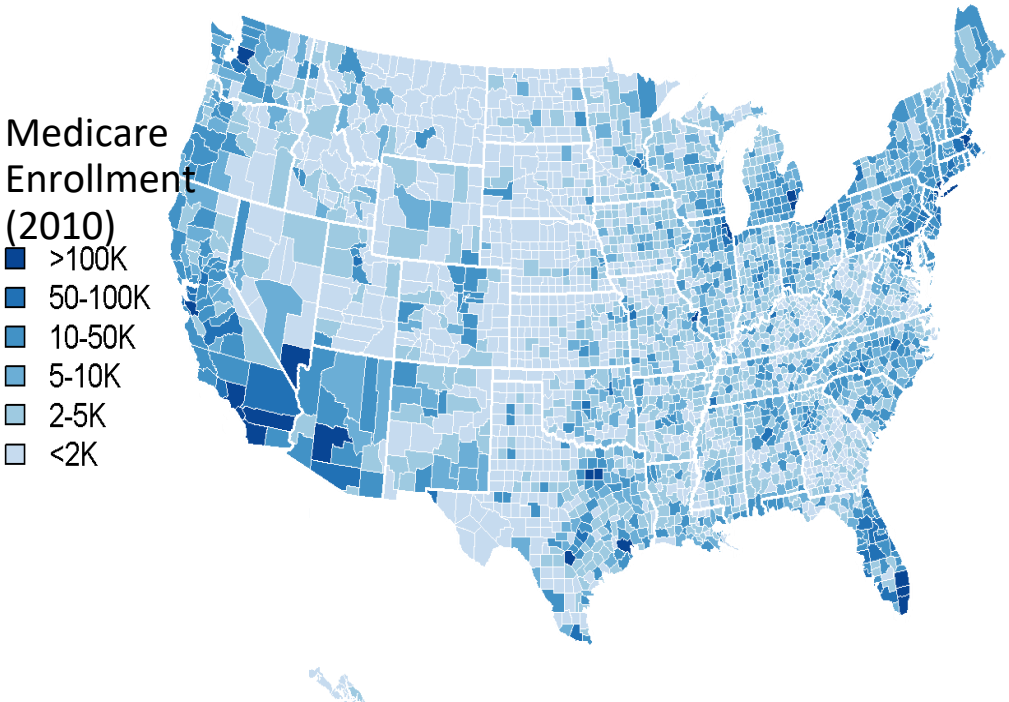
Source: Di et al. (2019a, 2019b); Requia et al. (2020)

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



Outcome assessment

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

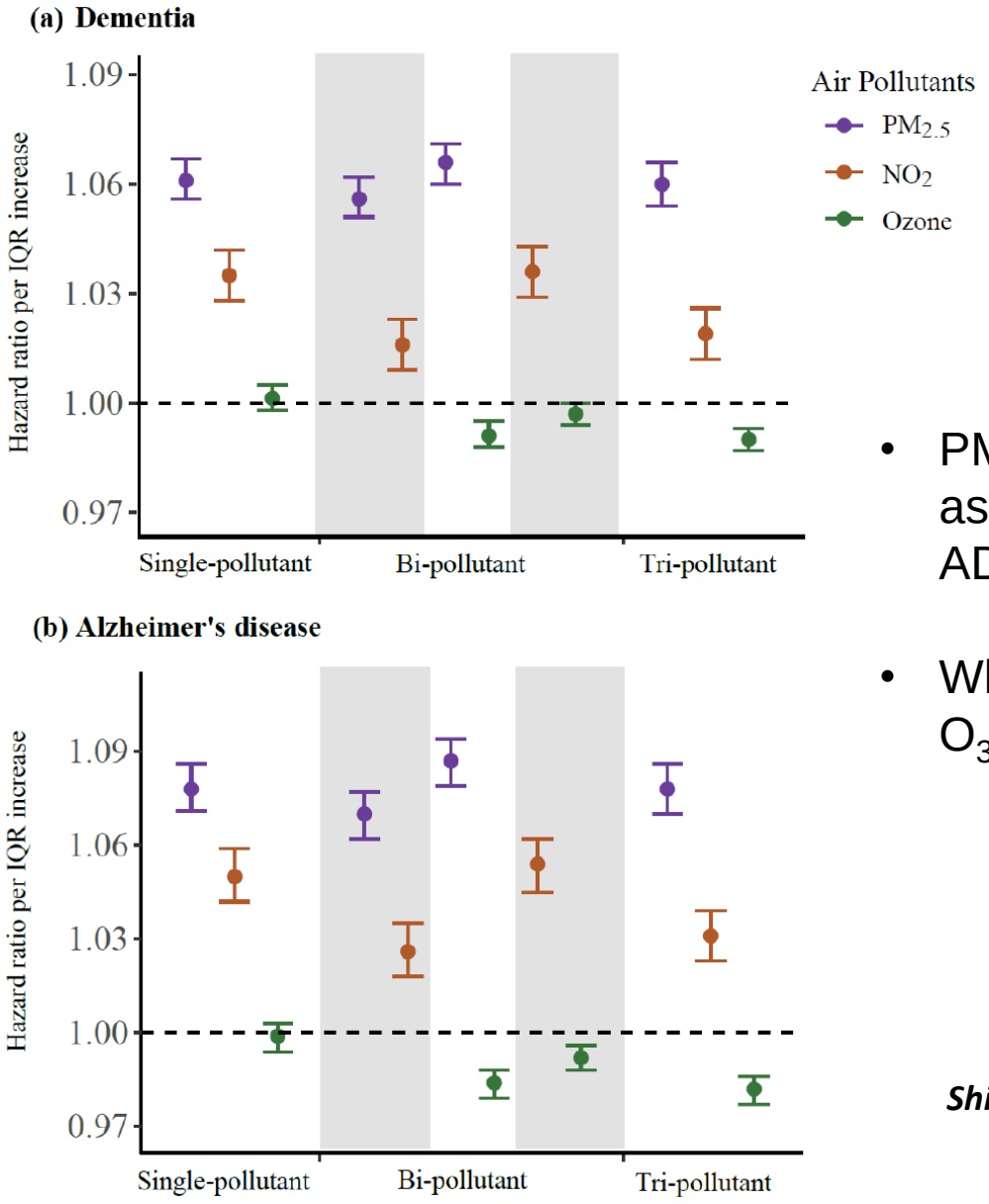
Cox proportional hazard model (survival analysis)

- 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)

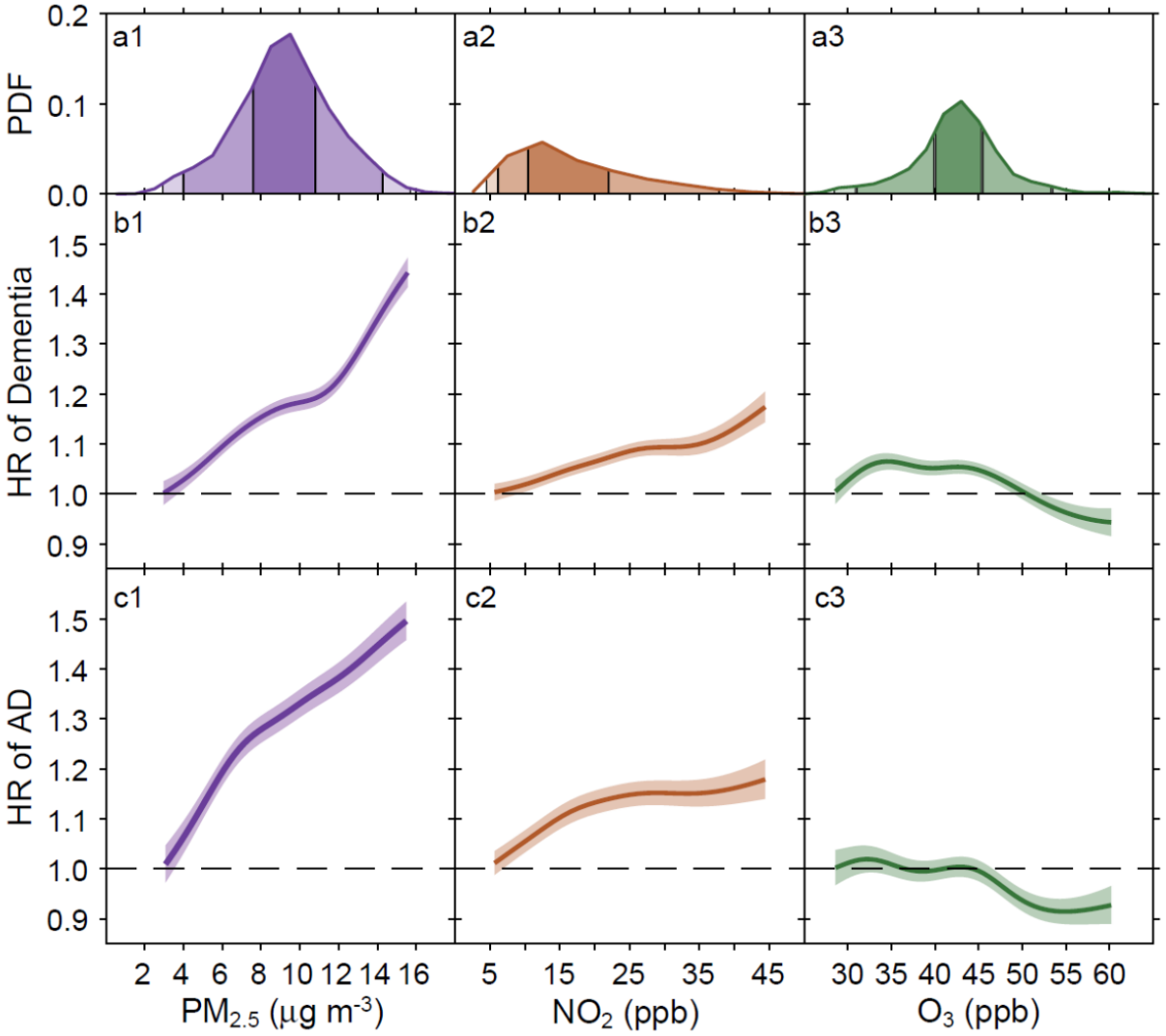
$PM_{2.5}$ and NO_2 are associated with incident dementia and AD



- $PM_{2.5}$ and NO_2 were significantly associated with incident dementia and AD.
- While hazard ratios for warm-season O_3 were not elevated

Shi et al., Nature Communications (2021)

Concentration-response (C-R) relationships

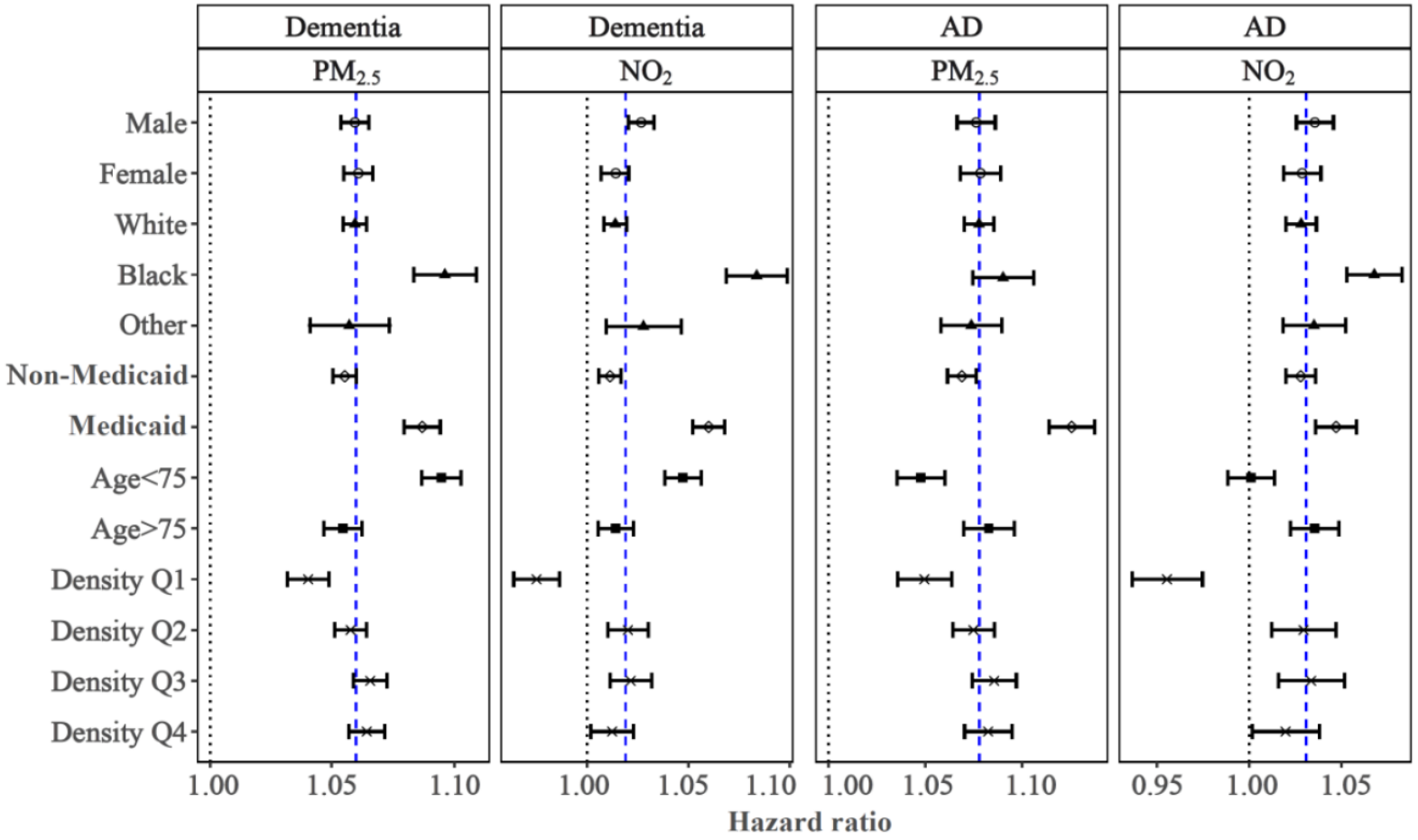


Dementia

AD

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*

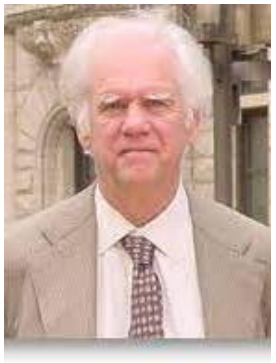
nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-021-27049-2 OPEN

A national cohort study (2000–2018) of long-term air pollution exposure and incident dementia in older adults in the United States

Liuhua Shi[1,9✉], Kyle Steenland[1,9], Haomin Li[2], Pengfei Liu[3], Yuhan Zhang[2], Robert H. Lyles[4], Weeberb J. Requia[5], Sindana D. Ilango[6], Howard H. Chang[1,4], Thomas Wingo[7], Rodney J. Weber[3] & Joel Schwartz[8]



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

Liuhua 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 Kioumourtzoglou†, Antonella Zanobetti†*

	AD	Dementia
Current study using Medicare CCW database (2000-2016)		
Number of admissions	5,646,187	11,121,272
Total person-years	403,149,214	379,921,997
Previous study* using Medicare inpatient claims (2000-2016)		
Number of admissions	2,490,431	1,233,132
Total person-years	475,820,277	478,636,053

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**

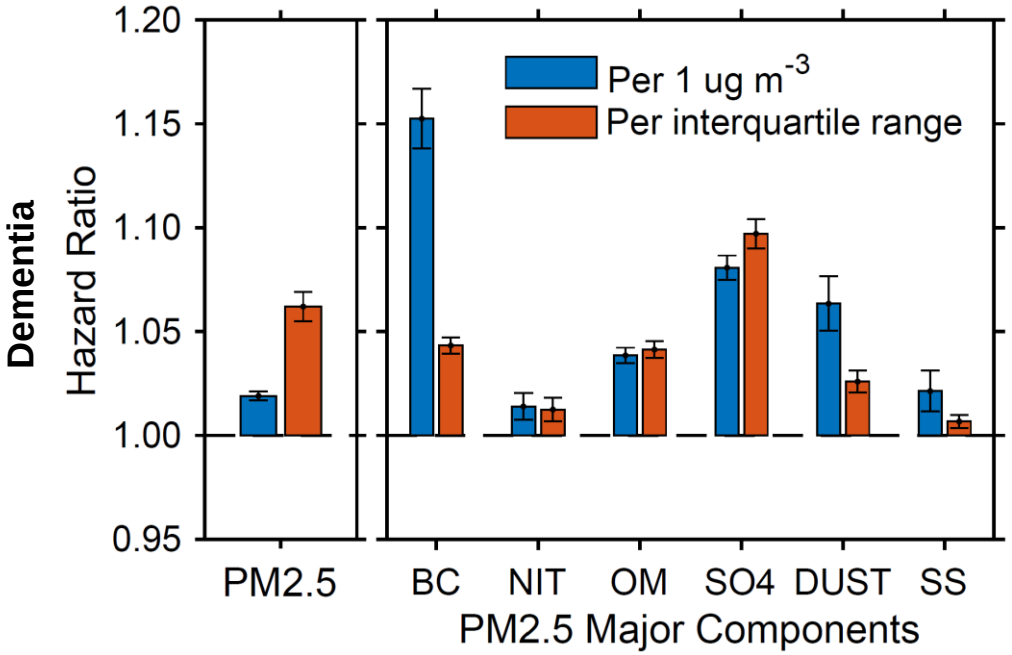
AD **5.6 million** **vs** **2.5 million**

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.

Preliminary results



Questions?

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