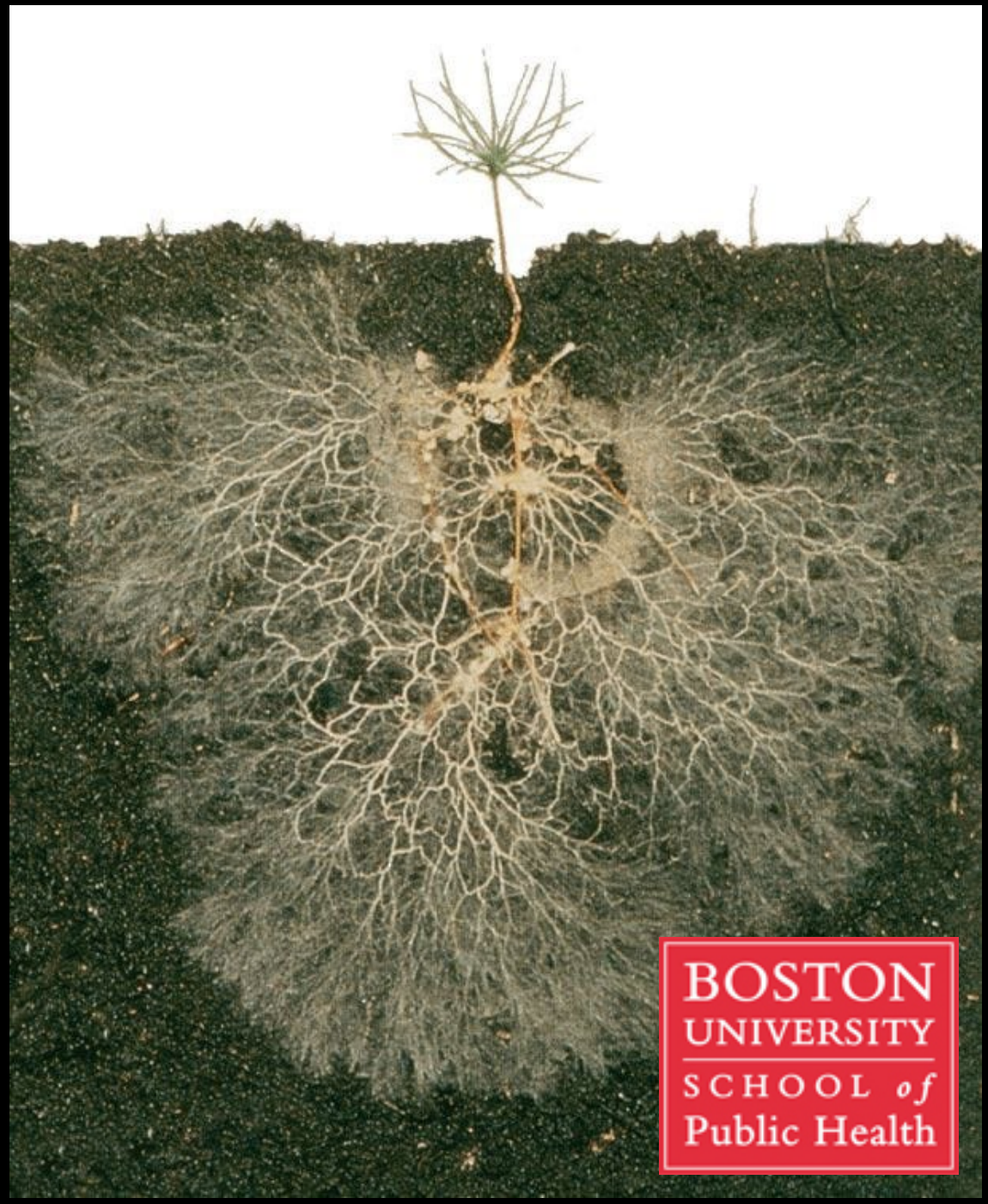
What epidemiologic evidence tells us *about the* contribution *of* air pollution *to* neurodegenerative etiology

Jennifer Weuve, MPH, ScD

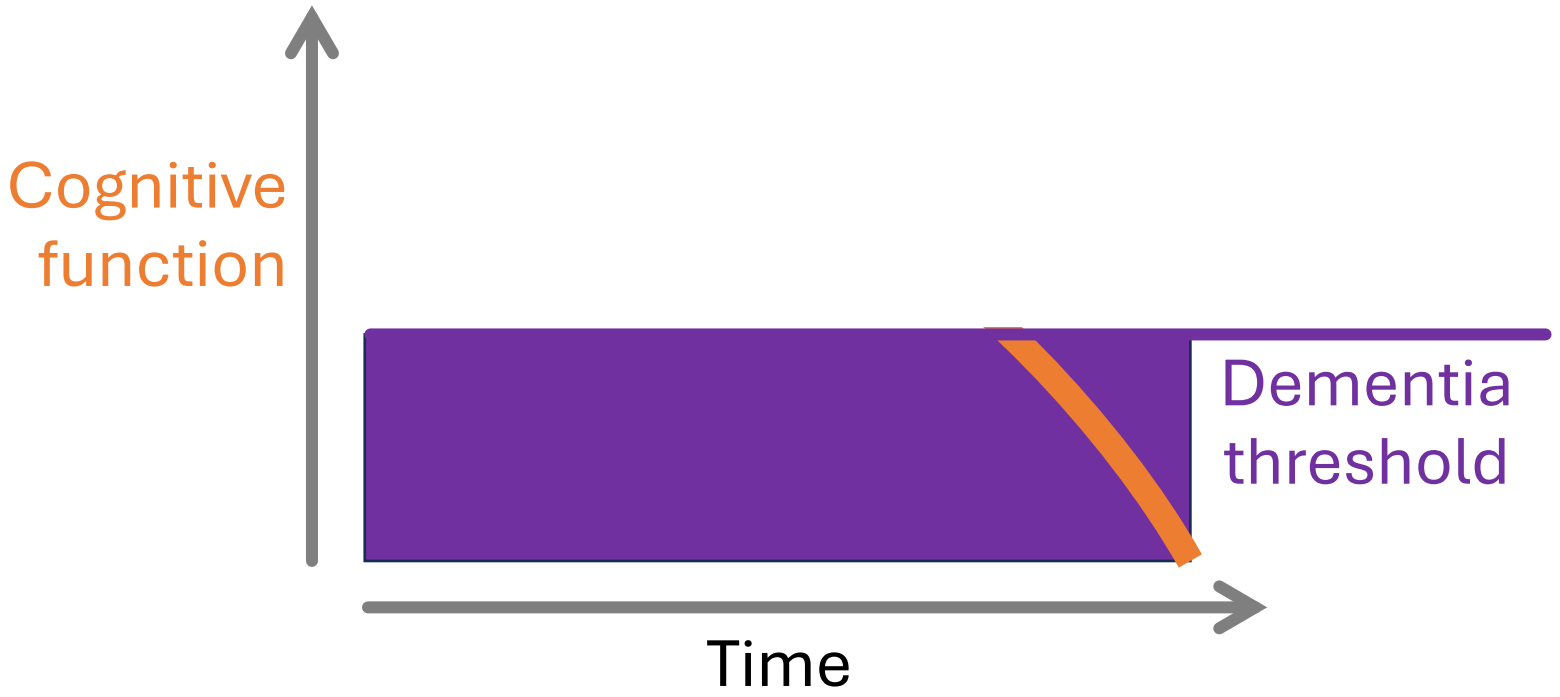
HEI's Annual Conference, 2026



Alzheimer’s disease, dementia, cognitive functioning, & cognitive decline

“Dementia”: a syndrome …

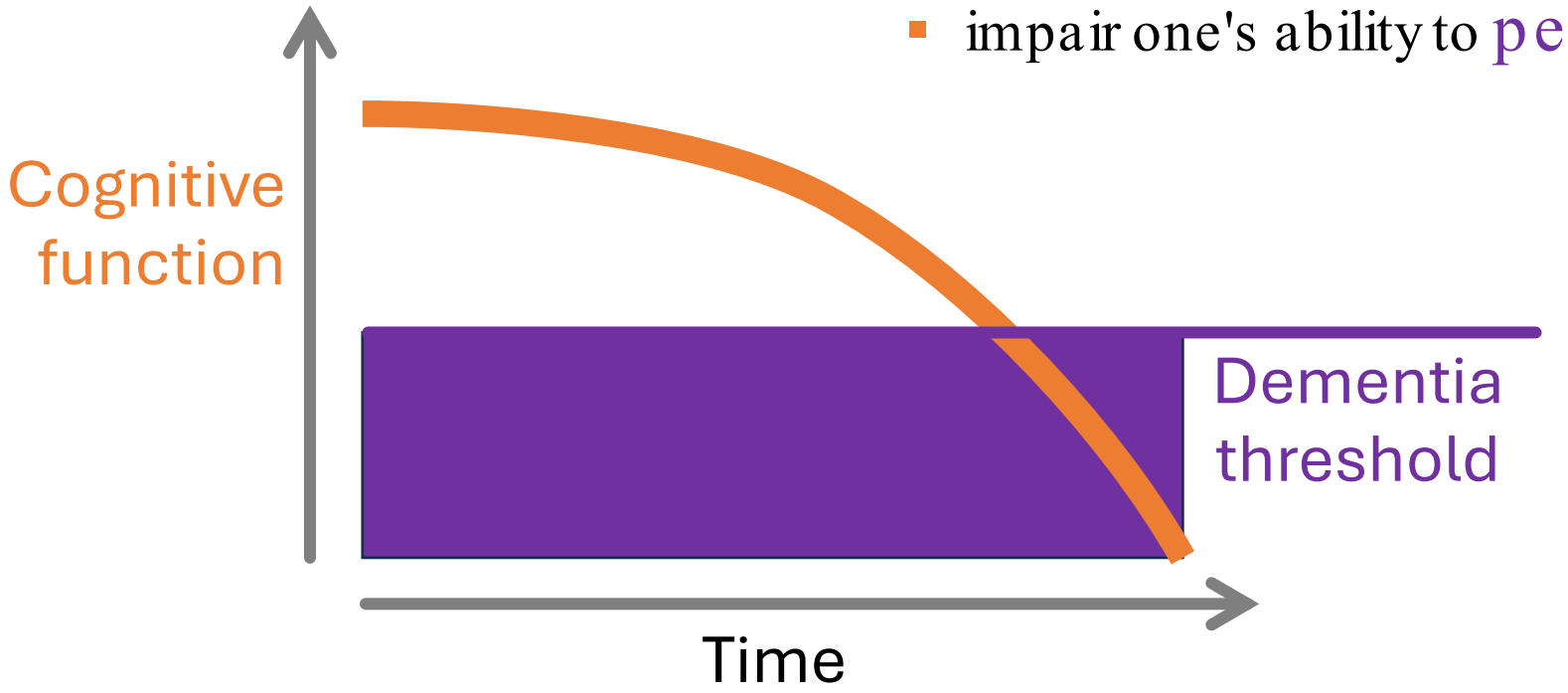
…defined by deficits in memory and other cognitive functions that:



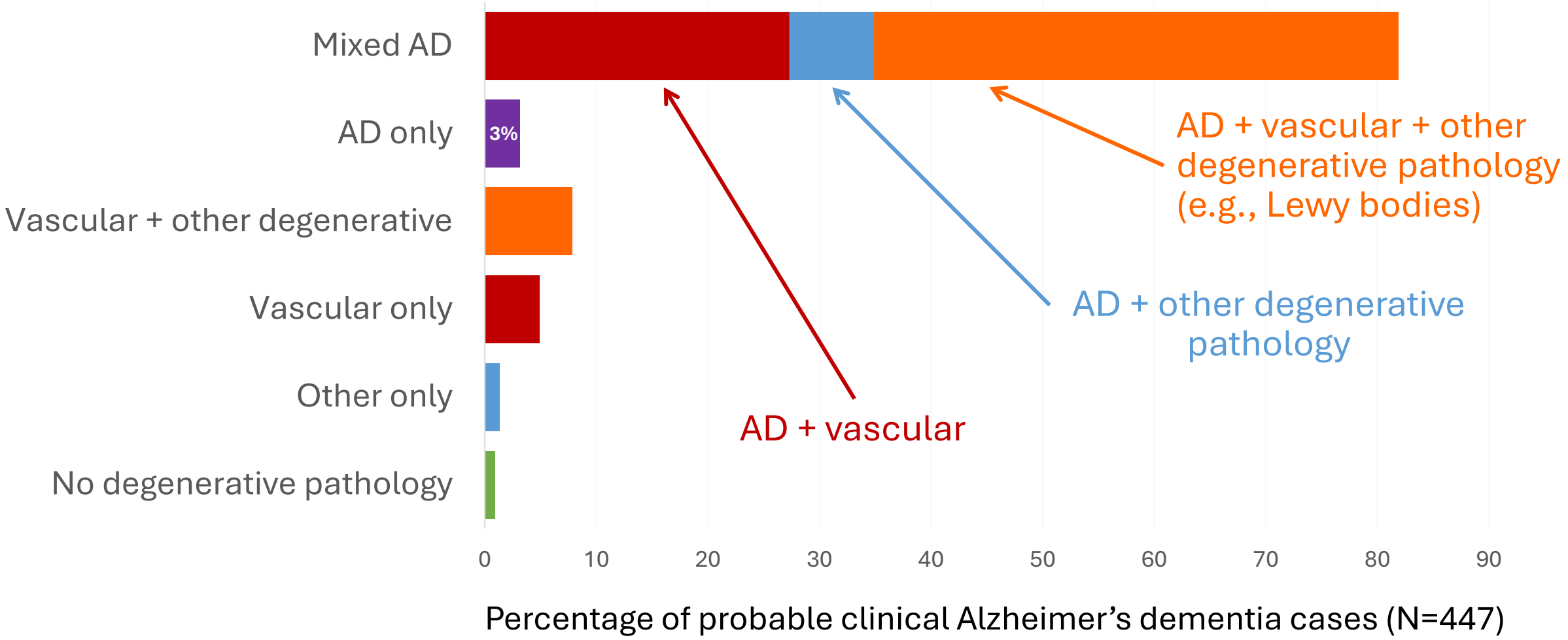
“Dementia”: a syndrome …

…defined by deficits in memory and other cognitive functions that:

- mark a decline from a previous level of functioning
- impair one's ability to perform everyday activities

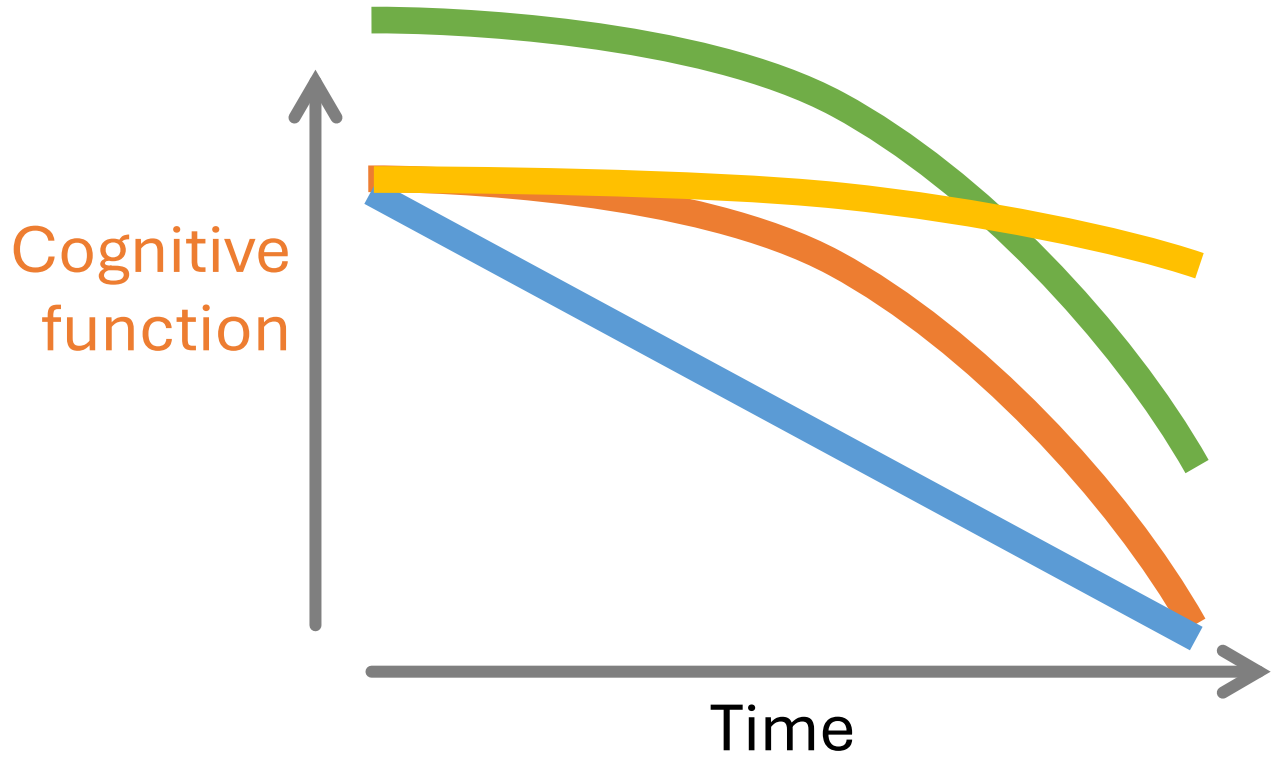


Alzheimer's disease neuropathology is common, but rarely occurs alone



Kapasi, DeCarli, & Schneider. *Acta Neuropathol*. 2017

Outcomes typically evaluated in research on the relation of air pollution to dementia



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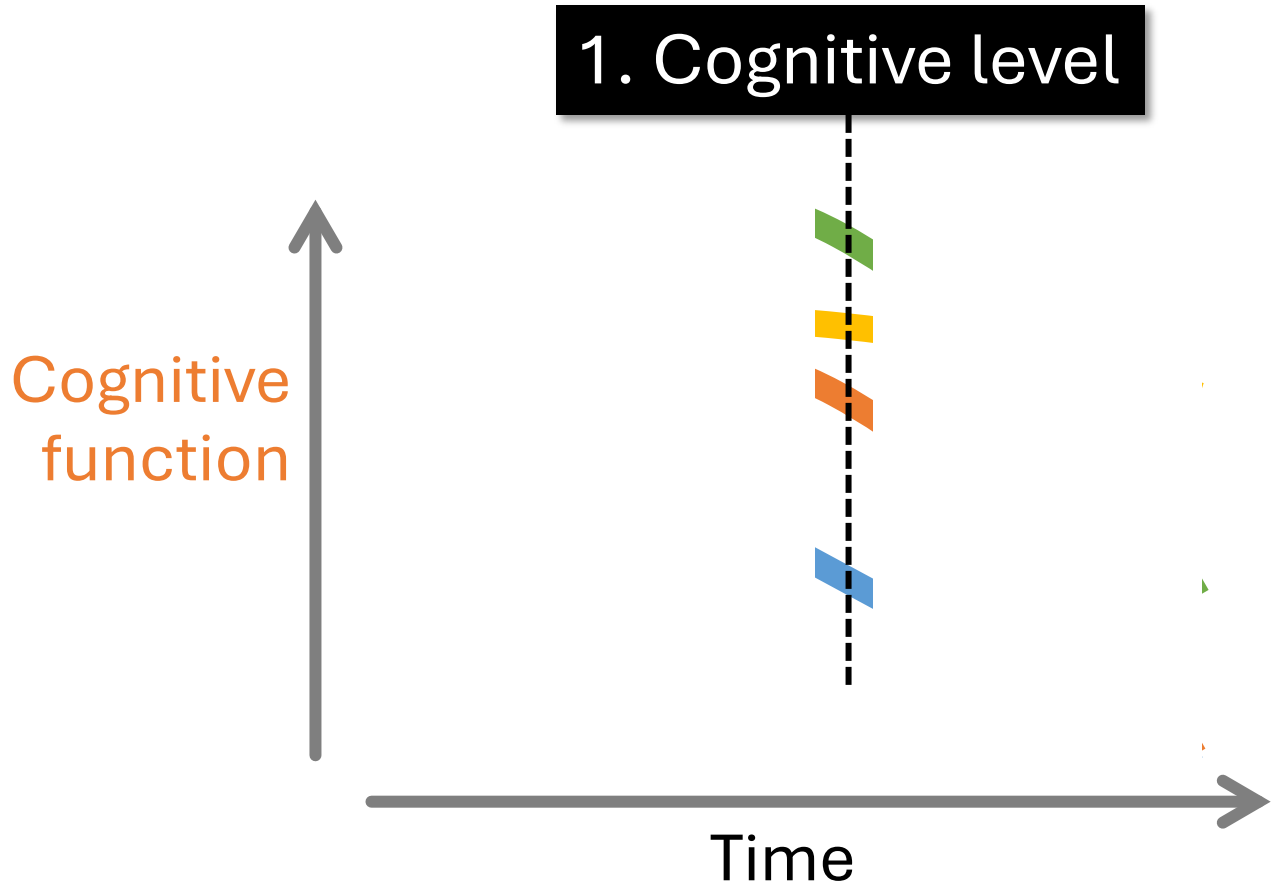

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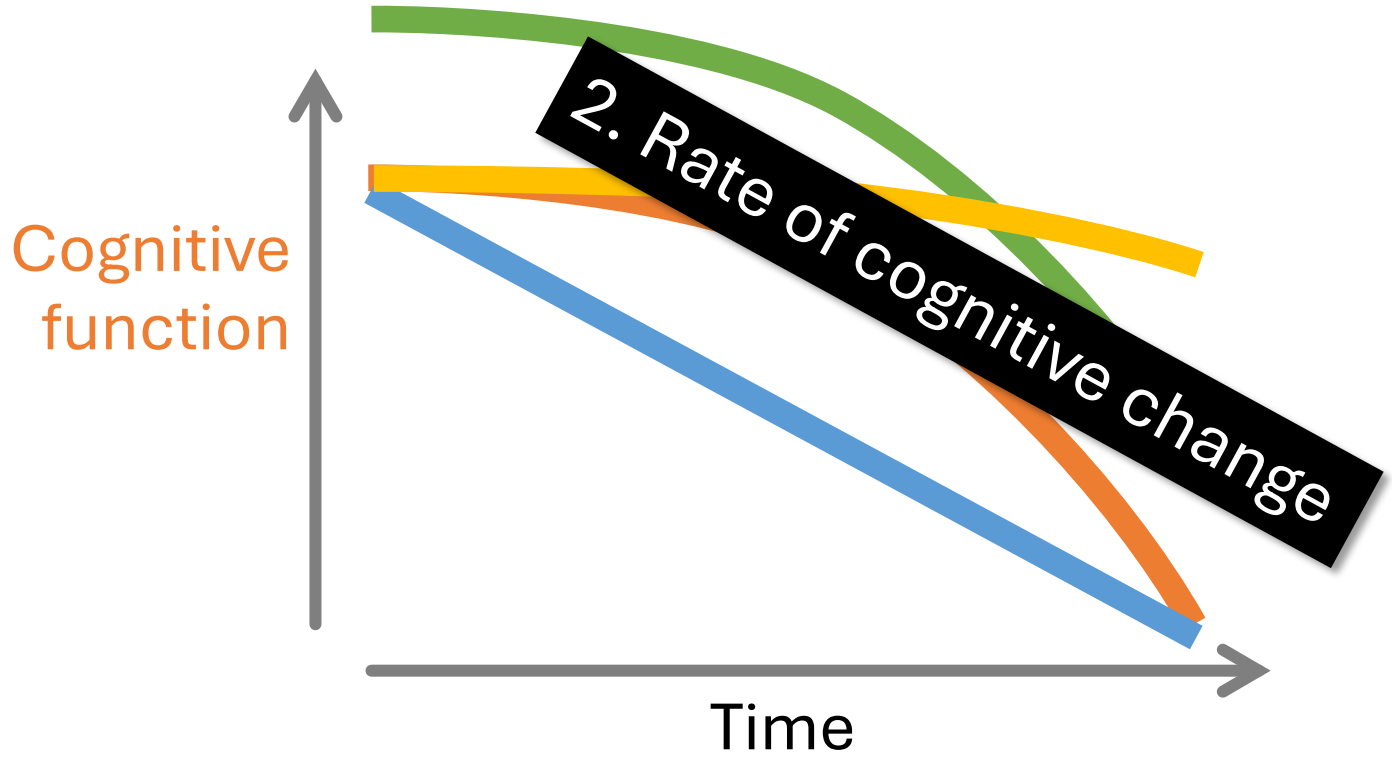

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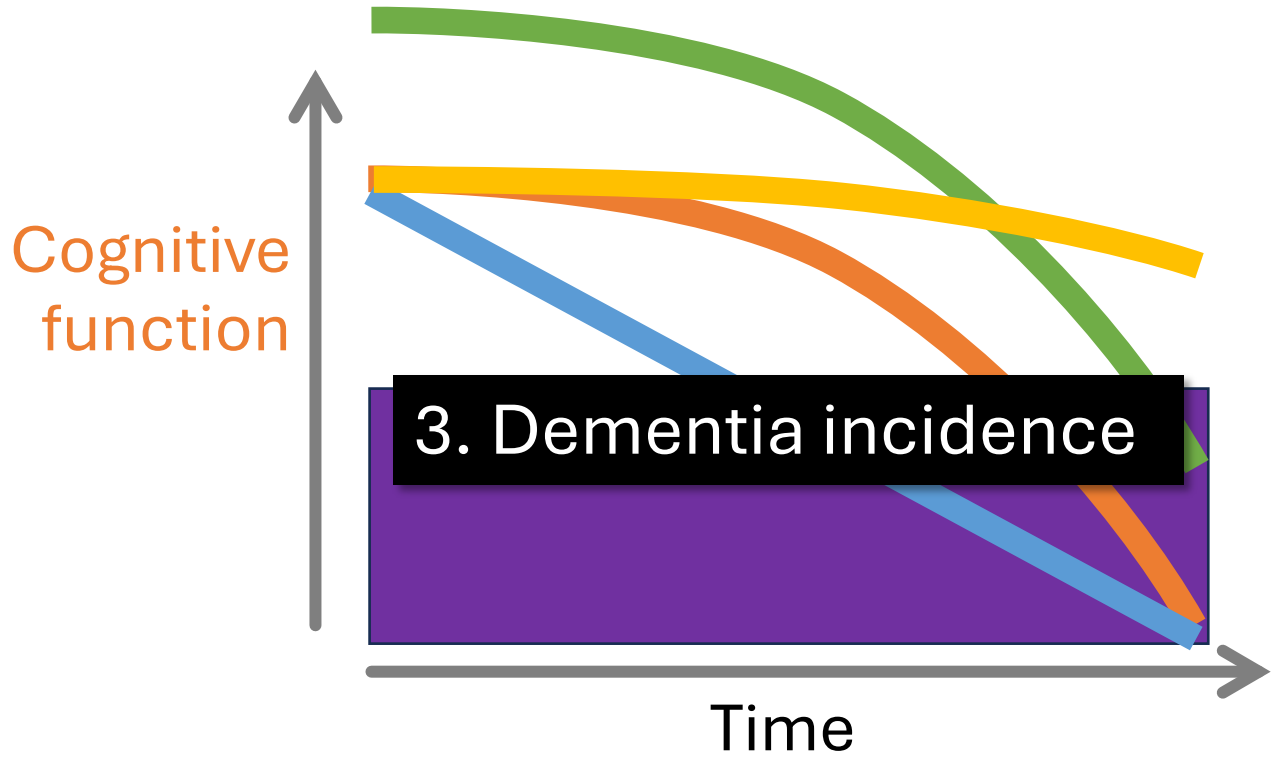
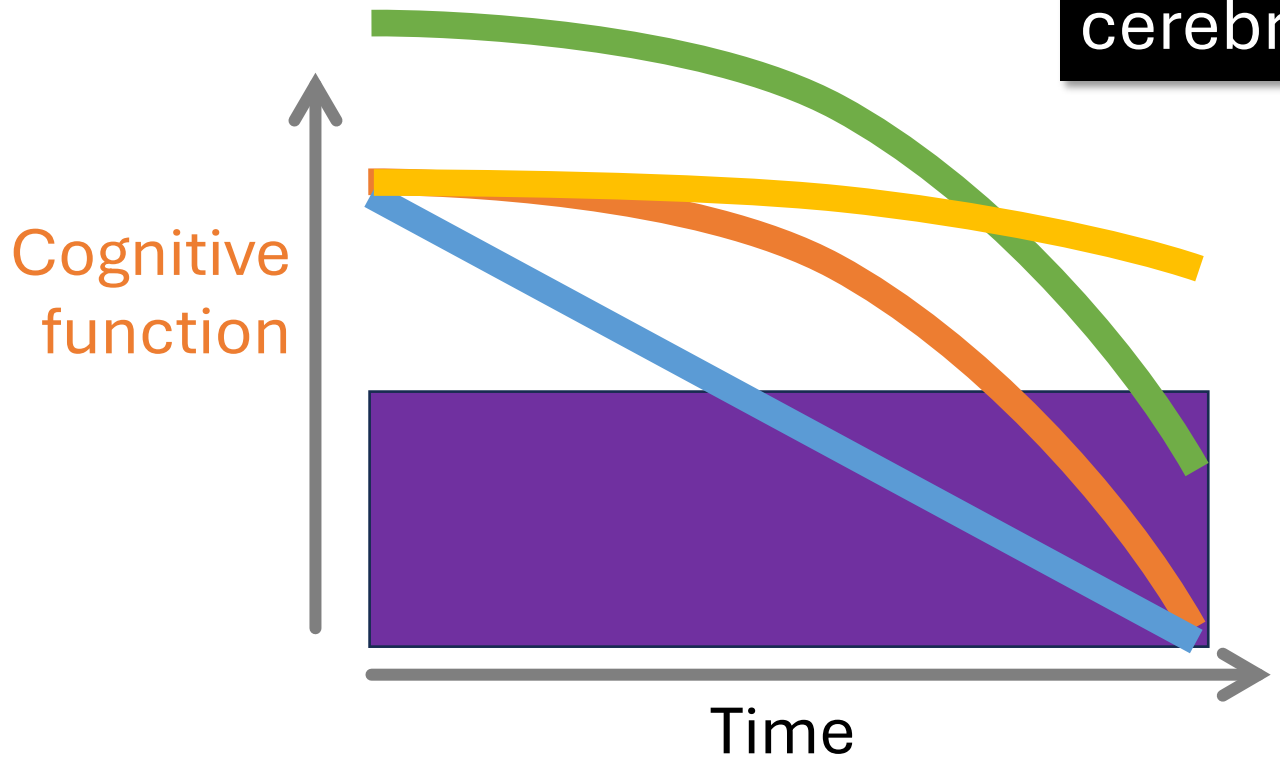


Outcomes typically evaluated in research on the relation of air pollution to dementia

4. CNS atrophy, cerebrovascular pathology



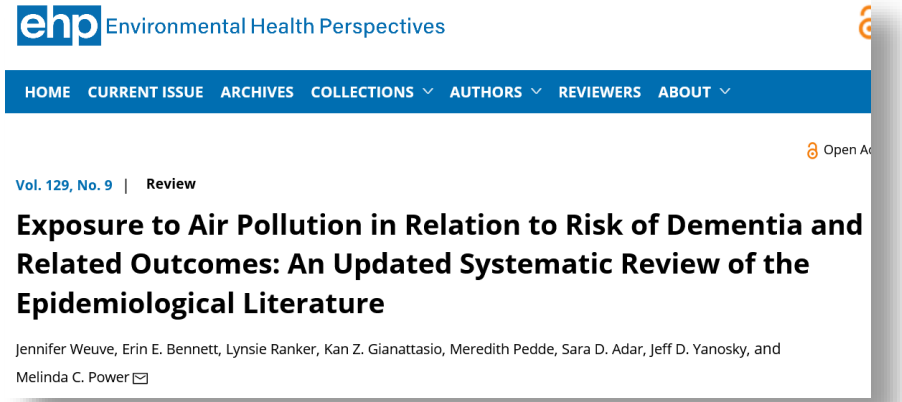
Created by Bambang Tirta Suganda from Noun Project

State of the epidemiologic science on air pollution and dementia

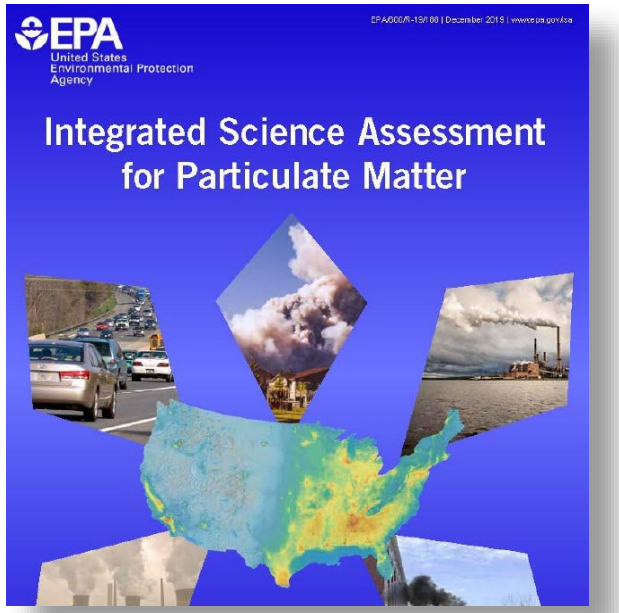
Jennifer Weuve, ScD jweuve@bu.edu

Sources

Systematic review:
Weuve et al. EHP (2021)



Systematic review: Wilker et al. BMJ (2023)



US EPA Integrated Science Assessment for Particulate Matter (2019)

CONCLUSIONS OF THESE REVIEWS

US EPA Integrated Science Assessment for PM (2019)

Long-term exposure to $PM_{2.5}$ is "likely to be causal" in relation to "nervous system effects."

Systematic review: Weuve et al. EHP (2021)

35 studies met quality review.

$PM_{2.5}$ → faster cognitive decline

Other evidence mixed or sparse.

Systematic review: Wilker et al. BMJ (2023)

16 studies (11 deemed high risk of bias)

$PM_{2.5}$ → ↑dementia risk
Less pronounced w admin records.

Other evidence mixed or sparse.

Recent developments in outcomes:

Does exposure to air pollution promote the neuropathology that underlies dementia?

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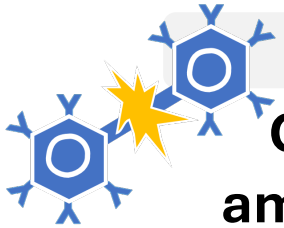
Emphasis has been on the pathology of AD (beta amyloid + pathologic tau)



	CSF MEASURES	
	Clearance of β-amyloid from brain	**Tau build-up in brain**
Chinese Longitudinal Healthy Longevity Survey (N=1131) (Ma, 2022)		
$PM_{2.5}$	impaired	build-up
NO_2	not reported	not reported
Ozone	not reported	not reported
Wisconsin Registry for Alzheimer's Prevention (N=795) (Kimura, 2026)		
$PM_{2.5}$	ø	build-up
Ozone	ø	build-up

But no assns of $PM_{2.5}$ or ozone with PET measures of β amyloid or tau

Autopsy studies of $PM_{2.5}$ and neuropathology of AD

STUDY	N	EXPOSURE PERIOD BEFORE DEATH	Estimated odds ratios (95% CI) per 1 µg/m³ $PM_{2.5}$		
			Neuropath AD	Beta amyloid 	Pathologic tau
ACT (Shaffer, 2021)	832	10 y	ABC Score **OR: 0.79** (0.49-1.19)	CERAD ***OR: 1.35** (0.90-1.90)	BRAAK stage ***OR: 0.99** (0.64-1.47)

* From ordinal logistic regression analyses.

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Penn (Kim, 2025)	602	1 y	ADNC score ***OR: 1.19** (1.11-1.28)	CERAD ***OR: 1.20** (1.11-1.30)	BRAAK stage ***OR: 1.20** (1.11-1.29)

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Emory (Chistensen, 2024)	224	1 y	ABC score ***OR: 1.45** (0.92-2.28)	CERAD ***OR: 1.92** (1.12–3.30)	BRAAK stage ***OR:1.15** (0.77-1.69)

* From ordinal logistic regression analyses.

Challenges in drawing inferences from autopsy studies of $PM_{2.5}$ and neuropathology of AD

- Selection bias
  - who **agrees to autopsy** and who **dies** and at what age
    - related to **dementia risk**
    - air pollution **exposure**, too?
  - **Clinical** vs **community** samples

ACT
ADULT CHANGES IN THOUGHT STUDY

Kaiser Permanente Washington Health Research Institute

Journal of Alzheimer's Disease
Volume 79, Issue 4, 2021, Pages 1761-1773

https://doi-org.ezproxy.bu.edu/10.3233/JAD-201005

SAGE journals

Research Article

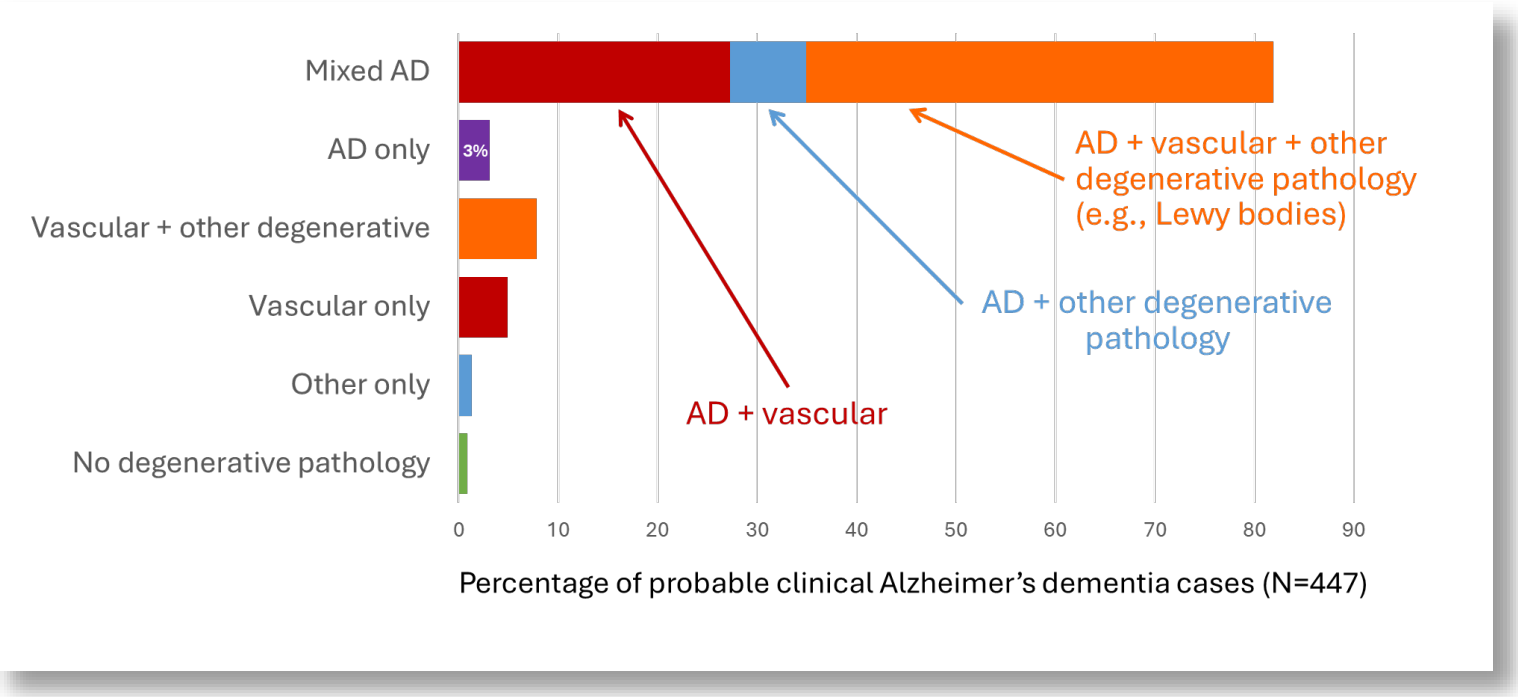
Fine Particulate Matter and Markers of Alzheimer's Disease Neuropathology at Autopsy in a Community-Based Cohort

Rachel M. Shaffer[a], Ge Li[b,c,d], Sara D. Adar[e], C. Dirk Keene[f], Caitlin S. Latimer[f], Paul K. Crane[g], Eric B. Larson[g,h], Joel D. Kaufman[a,i], Marco Carone[j], and Lianne Sheppard[a,j,*]

Challenges in drawing inferences from autopsy studies of $PM_{2.5}$ and neuropathology of AD

- **Exposure assessment**: is end of life the appropriate period?

- **Outcome assessment**: AD is not the *only* neuropathologic change that fuels dementia



Vascular, vascular, vascular

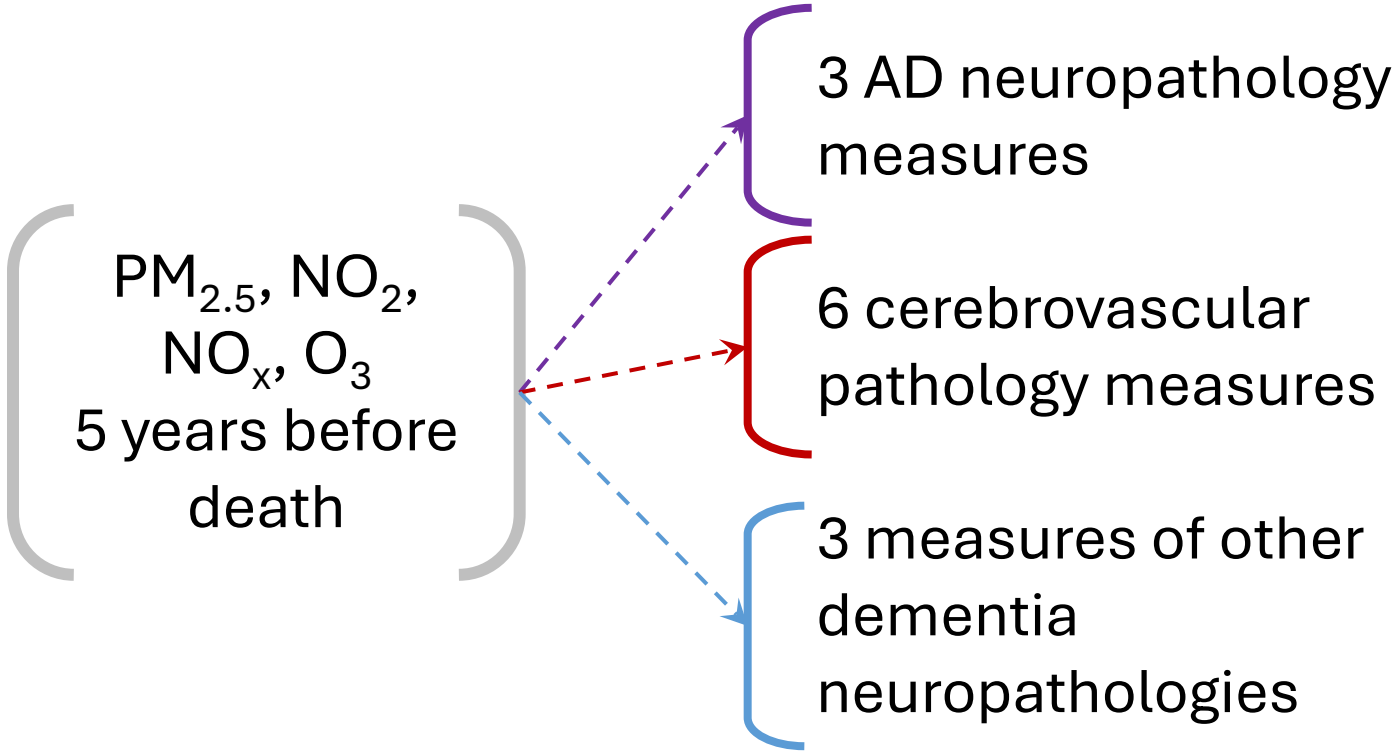
- Alzheimer-only dementias are rare
- Many (most?) people with dementia have cerebrovascular pathology
- Cerebrovascular pathology seems to potentiate AD pathology in manifesting symptoms
- Cognitive benefits of the US POINTER trial likely driven by vascular benefits (Schott JM. JAMA. 2025 PMID: 40720604).
- Air pollution has established cardiovascular effects

- But diagnosing "vascular dementia" is fraught with difficulty

Autopsy studies of air pollution and cerebrovascular pathology

AERONOSE

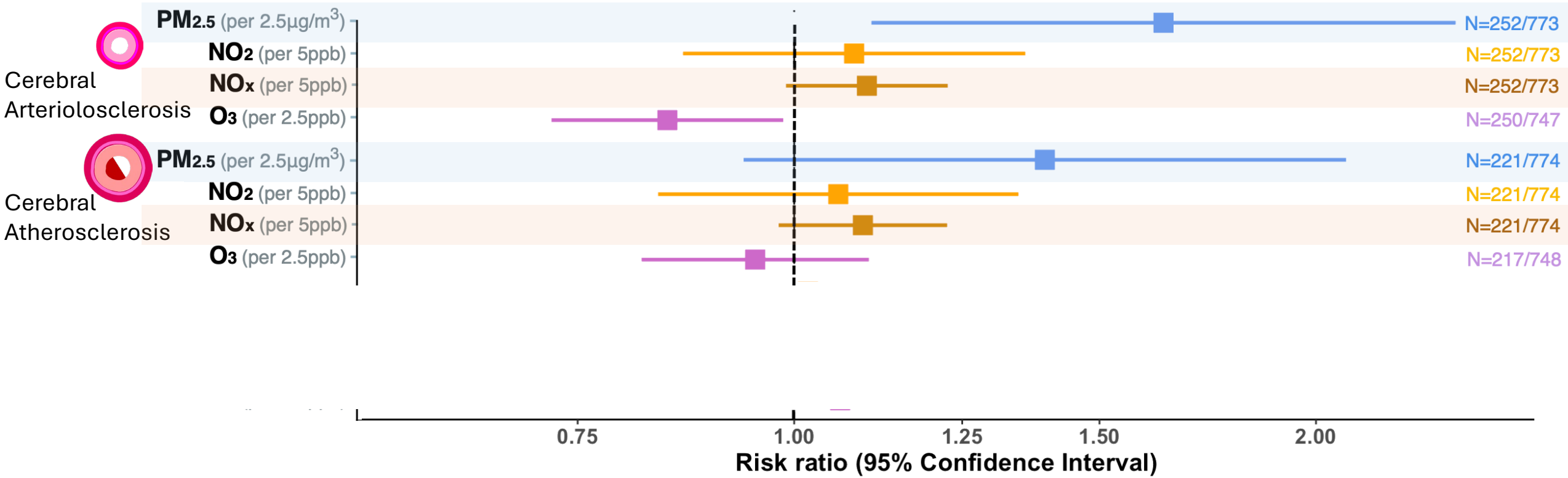
909 decedents from 4 community-based cohorts of the Rush Alzheimer's Disease Center



Jenson TE et al. medRxiv 2026.02.03.26345515; doi: https://doi.org/10.64898/2026.02.03.26345515. R01AG067497

Autopsy studies of air pollution and cerebrovascular pathology: AERONOSE

AERONOSE: Estimated cerebrovascular pathology prevalence ratios, using MESA Air's Chicago prediction models



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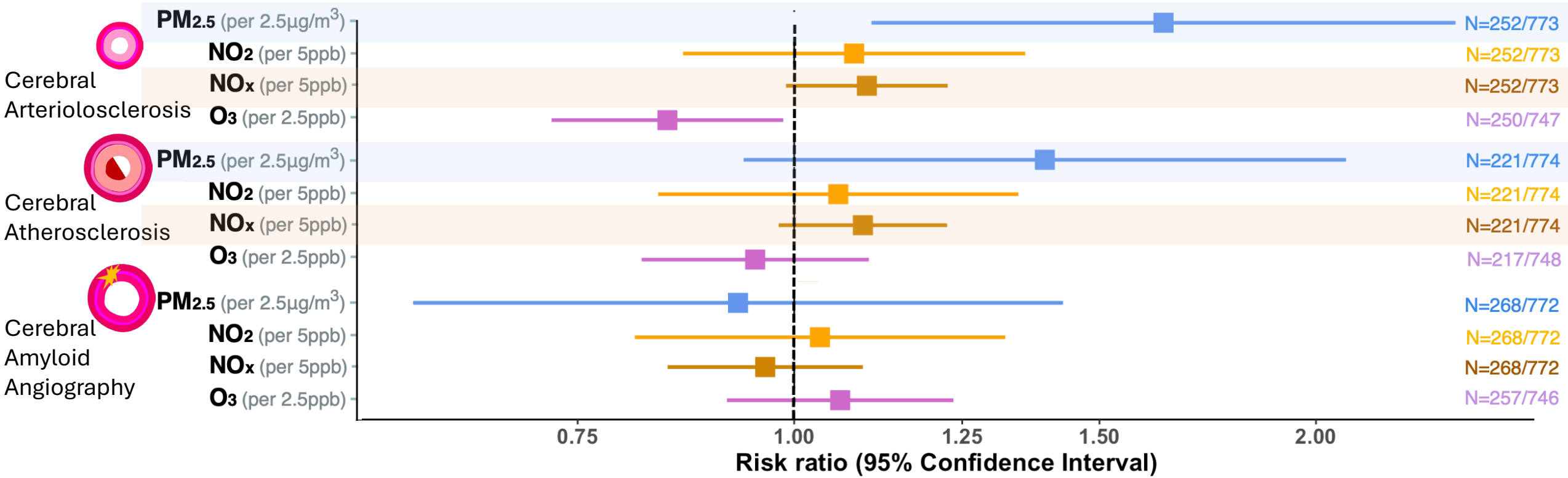

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Autopsy studies of air pollution and cerebrovascular pathology: Adult Changes in Thought

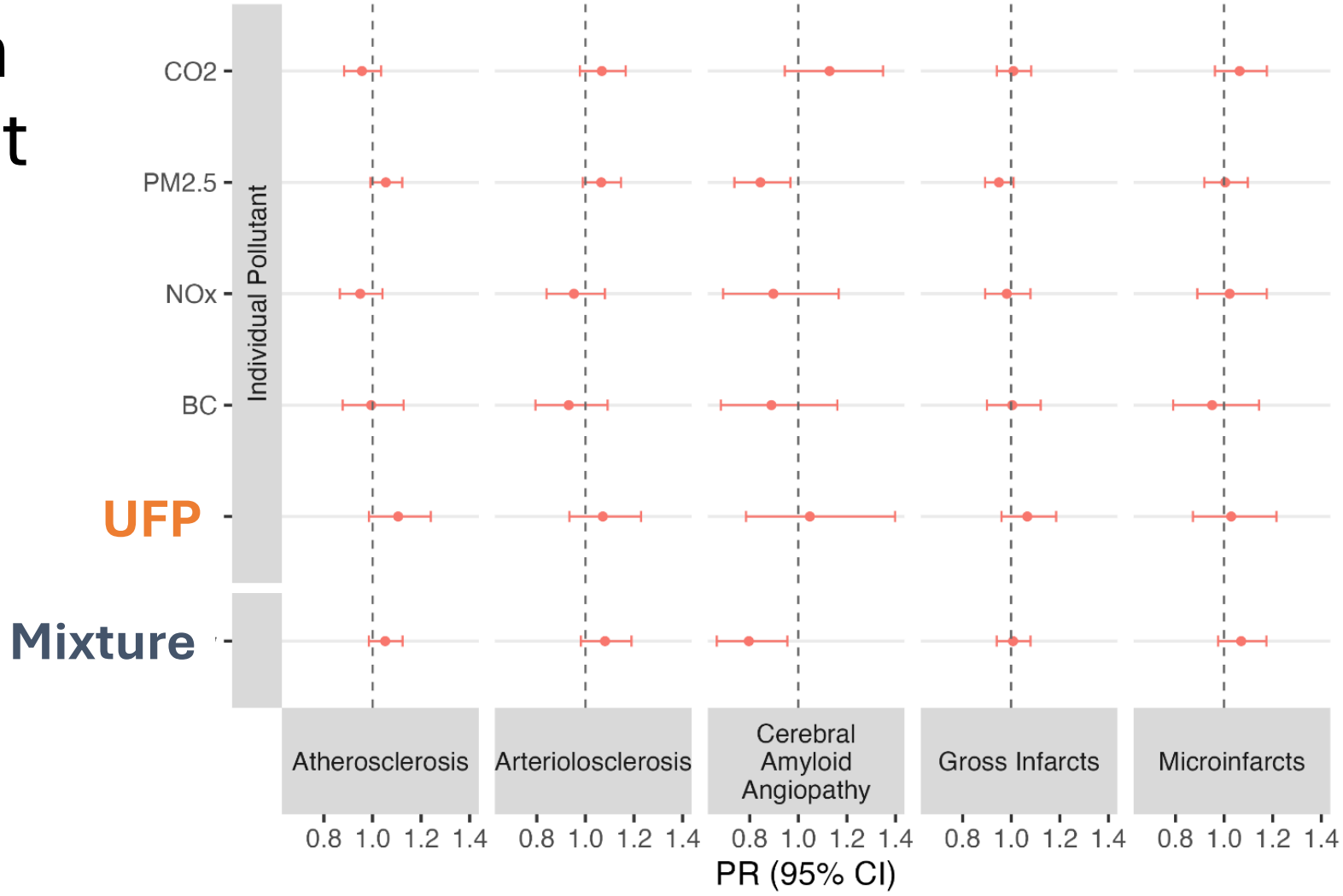
	Prevalence ratio (95% CI) per SD increment in 10-year air pollutant concentration	
	NOx (SD: 6 ppb)	**$PM_{2.5}$** (SD: 0.3 µg/m^3)
Cerebral Arteriolosclerosis	**0.95** (0.84-1.08)	**1.07** (0.99-1.15)
Cerebral Atherosclerosis	**0.95** (0.87-1.04)	**1.05** (0.99-1.12)
Cerebral amyloid angiography	**0.90** (0.69-1.17)	**0.84** (0.74-0.97)

Blanco MN et al. See her poster here at the conference!

Recent developments on exposure

Jennifer Weuve, ScD jweuve@bu.edu

Emerging research on UFPs and air pollutant mixtures: Adult Changes in Thought



Blanco MN et al. See her poster here at the conference!

Sources of $PM_{2.5}$ in relation to dementia risk: Health and Retirement Study (U.S.)

In a study by Zhang et al (2023):

- 10-year mean exposures to total $PM_{2.5}$ and $PM_{2.5}$ from 9 sources estimated for 27,857 participants …

Research

JAMA Internal Medicine | Original Investigation

Comparison of Particulate Air Pollution From Different Emission Sources and Incident Dementia in the US

Boya Zhang, PhD; Jennifer Weuve, ScD; Kenneth M. Langa, MD, PhD; Jennifer D'Souza, PhD; Adam Szpiro, PhD; Jessica Faul, PhD; Carlos Mendes de Leon, PhD; Jiaqi Gao, MPH; Joel D. Kaufman, MD; Lianne Sheppard, PhD; Jinkook Lee, PhD; Lindsay C. Kobayashi, PhD; Richard Hirth, PhD; Sara D. Adar, ScD

Zhang et al. JAMA Int Med 2023

Hazard ratios (95% CIs) of incident dementia per interquartile increment in 10-year mean concentration of source-specific fine particulate matter ($PM_{2.5}$)

Source (IQR)	HR (95% CI)
Total $PM_{2.5}$ (9.5-13.2)	
Model 1	1.08 (1.01-1.17)
Model 3	1.12 (1.02-1.24)
Agriculture (0.6-1.7)	
Model 1	1.17 (1.05-1.30)
Model 2	1.13 (1.01-1.27)
Model 3	1.12 (0.98-1.27)
Road traffic (1.1-1.7)	
Model 1	1.11 (1.01-1.23)
Model 2	1.06 (0.94-1.19)
Model 3	1.03 (0.91-1.17)
Nonroad traffic (0.3-0.5)	
Model 1	1.14 (1.00-1.32)
Model 2	1.07 (0.92-1.26)
Model 3	1.07 (0.91-1.25)
Energy coal (0.5-1.1)	
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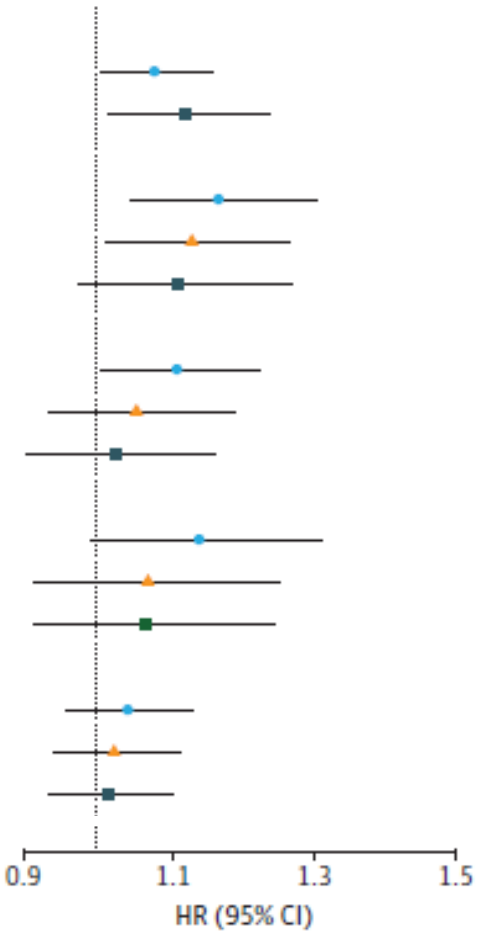
Model 3	1.02 (0.93-1.11)



Zhang et al. JAMA Int Med 2023

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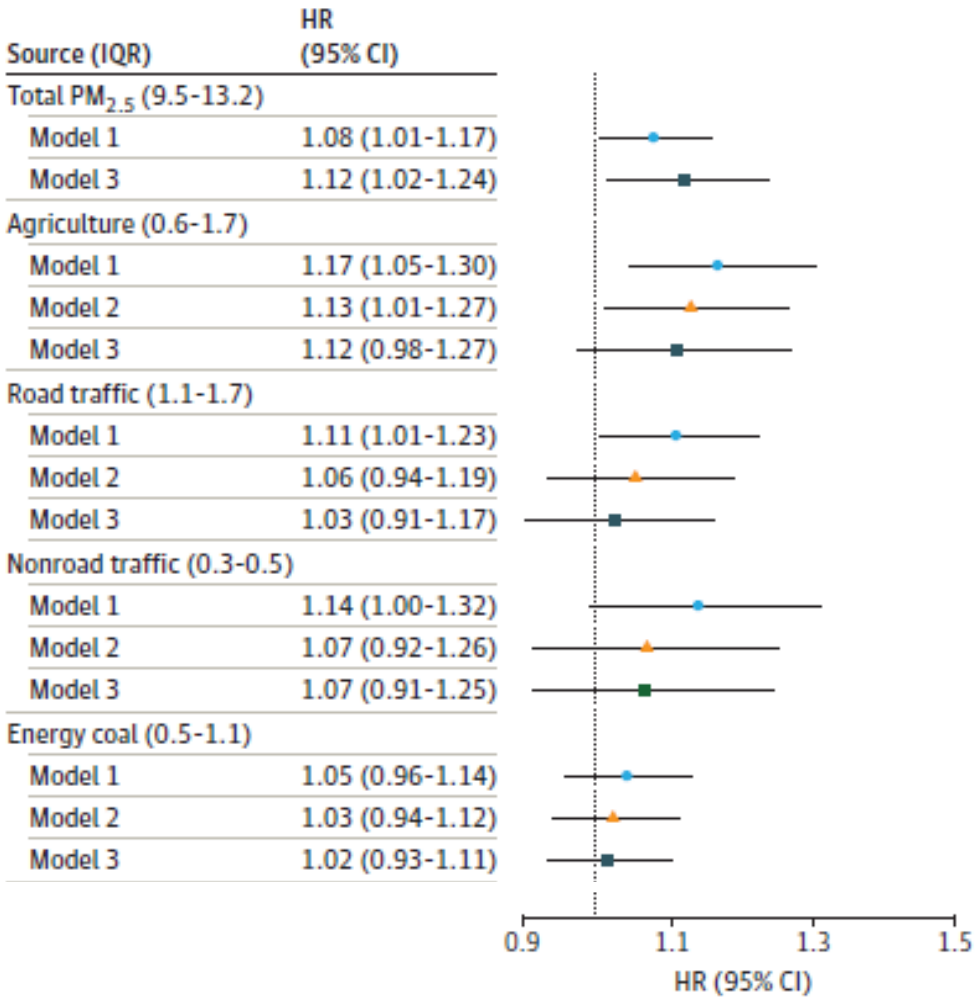

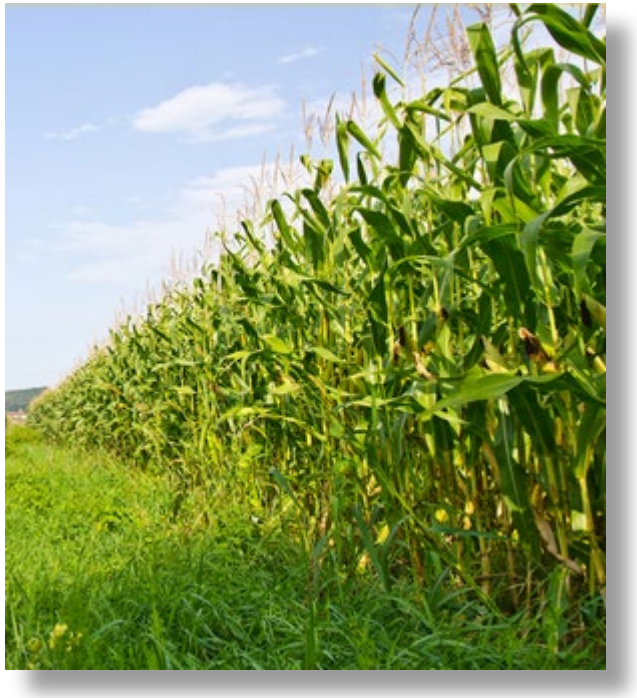

Zhang et al. JAMA Int Med 2023

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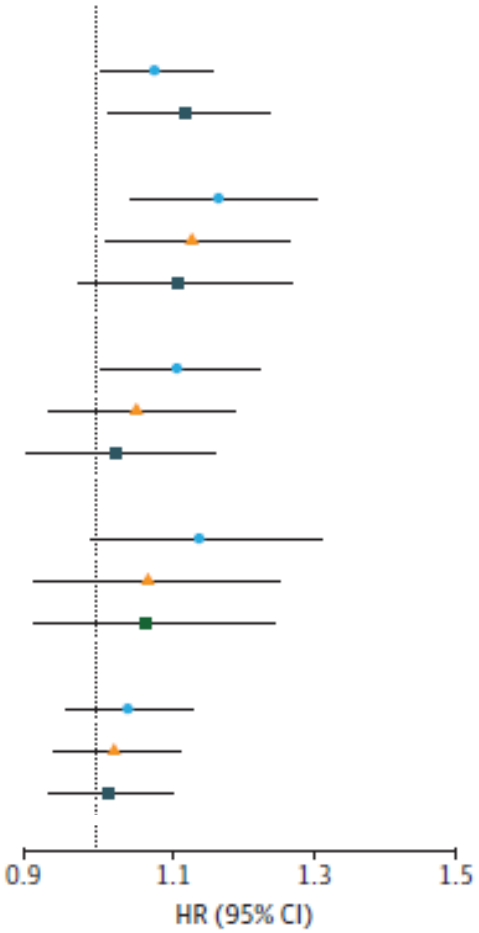

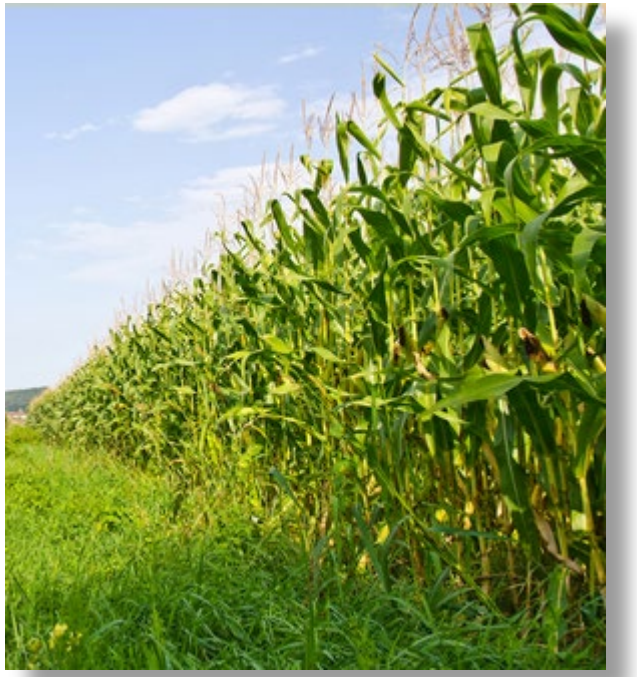

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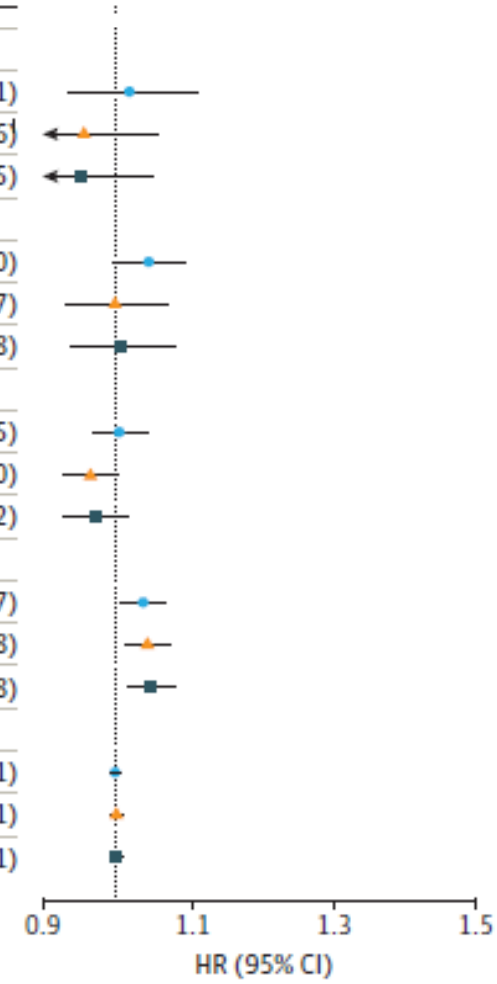
Model 1	1.08 (1.01-1.17)
Model 3	1.12 (1.02-1.24)
Agriculture (0.6-1.7)	

Source (IQR)	HR (95% CI)
Energy other (0.4-0.7)	
Model 1	1.02 (0.93-1.11)
Model 2	0.96 (0.87-1.06)
Model 3	0.95 (0.86-1.05)
Industry coal (0.2-0.3)	
Model 1	1.05 (1.00-1.10)
Model 2	1.00 (0.93-1.07)
Model 3	1.01 (0.94-1.08)
Industry other (0.7-1.2)	
Model 1	1.01 (0.97-1.05)
Model 2	0.97 (0.93-1.00)
Model 3	0.97 (0.93-1.02)
Wildfires (0.7-1.3)	
Model 1	1.04 (1.01-1.07)
Model 2	1.05 (1.02-1.08)
Model 3	1.05 (1.02-1.08)
Windblown dust (0.0-0.1)	
Model 1	1.00 (0.99-1.01)
Model 2	1.00 (1.00-1.01)
Model 3	1.00 (0.99-1.01)



Zhang et al. JAMA Int Med 2023

Other evidence on wildfire air pollution

- Study of 1.28M members of Kaiser Permanente Southern California (Elser, 2025).
  - Per 1-μg/m^3 increment in 3-year mean of:
    - wildfire $PM_{2.5}$ exposure, dementia OR=1.12 (95% CI, 0.98-1.28)
    - <u>non</u>wildfire $PM_{2.5}$ exposure, dementia OR=1.007 (95% CI, 1.002-1.011)

- Study of 5,699 participants of LASI-DAD in India (Zhang, 2025).
  - Exposure to wildfire $PM_{2.5}$ was:
    - Not associated with cognitive performance
    - Associated with slower rate of cognitive decline

What epidemiologic evidence tells us *about the* contribution *of* air pollution *to* neurodegenerative etiology

Jennifer Weuve, MPH, ScD

HEI's Annual Conference, 2026