ACT Symposium
May 13th, 2025

ADRD Neuropathologies and Exposure to Air Pollution Mixtures in ACT

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Agenda

BACKGROUND

AIR POLLUTION MIXTURES AND NEUROPATHOLOGY

PLANNED WORK

Agenda

BACKGROUND

AIR POLLUTION MIXTURES AND NEUROPATHOLOGY

PLANNED WORK

Air Pollution

$PM_{2.5}$

NO_x

UFP

SO_2

BC

O_3

CO_2

VOCs

https://deohs.washington.edu/healthy-air-healthy-schools-technical-information

Literature Linking Air Pollution to Clinical Cognitive Outcomes

Review

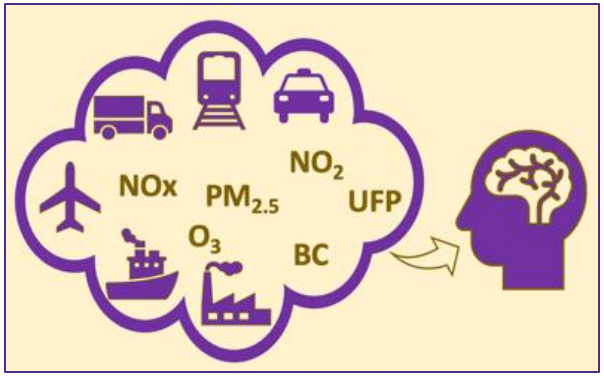
A Section 508-conformant HTML version of this article is available at https://doi.org/10.1289/EHP8716.

Exposure to Air Pollution in Relation to Risk of Dementia and Related Outcomes: An Updated Systematic Review of the Epidemiological Literature

Jennifer Weuve,[1] Erin E. Bennett,[2] Lynsie Ranker,[1] Kan Z. Gianattasio,[2] Meredith Pedde,[3] Sara D. Adar,[3] Jeff D. Yanosky,[4] and Melinda C. Power[2]

Dementia prevention, intervention, and care: 2024 report of the *Lancet* standing Commission

Gill Livingston, Jonathan Huntley, Kathy Y Liu, Sergi G Costafreda, Geir Selbæk, Suvarna Alladi, David Ames, Sube Banerjee, Alistair Burns, Carol Brayne, Nick C Fox, Cleusa P Ferri, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Noeline Nakasujja, Kenneth Rockwood, Quincy Samus, Kokoro Shirai, Archana Singh-Manoux, Lon S Schneider, Sebastian Walsh, Yao Yao, Andrew Sommerlad, Naaheed Mukadam**



Review Article

The emerging risk of exposure to air pollution on cognitive decline and Alzheimer's disease – Evidence from epidemiological and animal studies

*Jason Kilian, Masashi Kitazawa**

Research

A Section 508-conformant HTML version of this article is available at https://doi.org/10.1289/EHP9018.

Fine Particulate Matter and Dementia Incidence in the Adult Changes in Thought Study

Rachel M. Shaffer,[1] Magali N. Blanco,[1] Ge Li,[2,3,4] Sara D. Adar,[5] Marco Carone,[6] Adam A. Szpiro,[6] Joel D. Kaufman,[6,7] Timothy V. Larson,[1,8] Eric B. Larson,[9,10] Paul K. Crane,[9] and Lianne Sheppard[1,6]

Review article

Exposure to air pollution and cognitive functioning across the life course – A systematic literature review

Angela Clifford [a], Linda Lang [a,b], Ruoling Chen [a,b,*], Kaarin J. Anstey [c], Anthony Seaton [d]

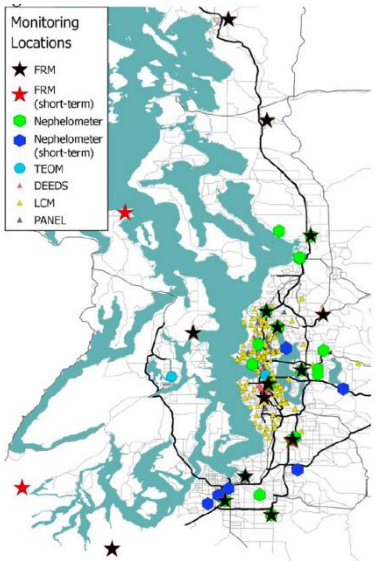
Full length article

Traffic-related air pollution and dementia incidence in the Adult Changes in Thought Study

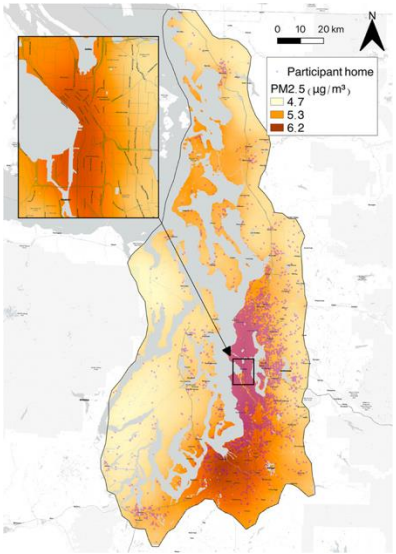
Magali N. Blanco [a,*], Rachel M. Shaffer [a], Ge Li [b,c,d], Sara D. Adar [e], Marco Carone [f], Adam A. Szpiro [f], Joel D. Kaufman [a,g,h], Timothy V. Larson [a,i], Anjum Hajat [g], Eric B. Larson [h], Paul K. Crane [h], Lianne Sheppard [a,f]

$PM_{2.5}$ and Dementia Incidence in ACT

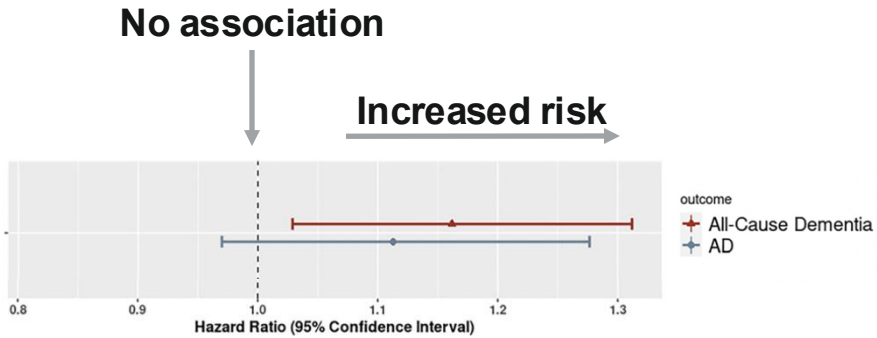
Shaffer, PhD



Historical $PM_{2.5}$ measurements, 1978+



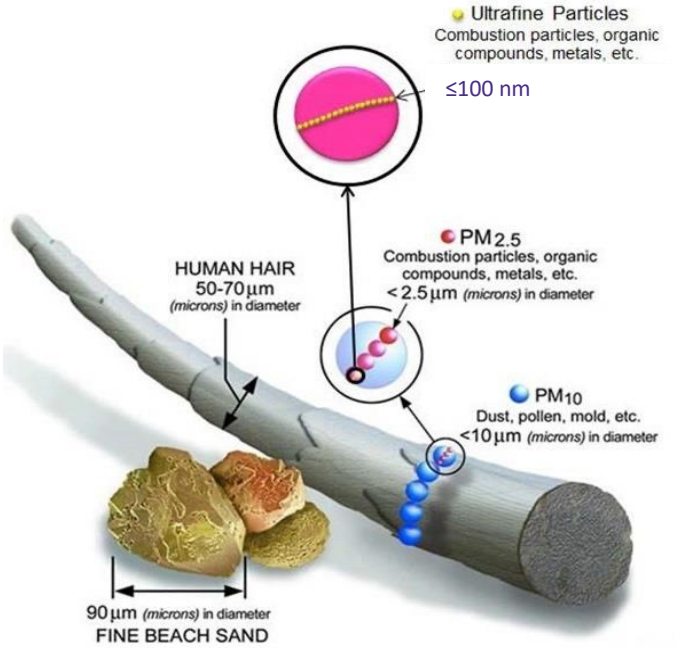
Predicted 10yr average $PM_{2.5}$ for 2000-2009

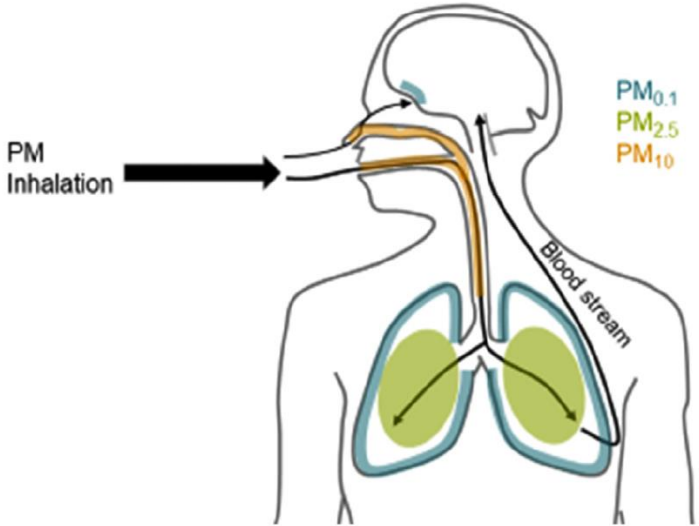


Adjusted all-cause dementia HR: 1.16 (95% CI: 1.03, 1.31) per 1 µg/m^3 increment of $PM_{2.5}$.

Shaffer et al. 2021. EHP. *Fine particulate matter and dementia in ACT.* DOI: 10.1289/EHP9018

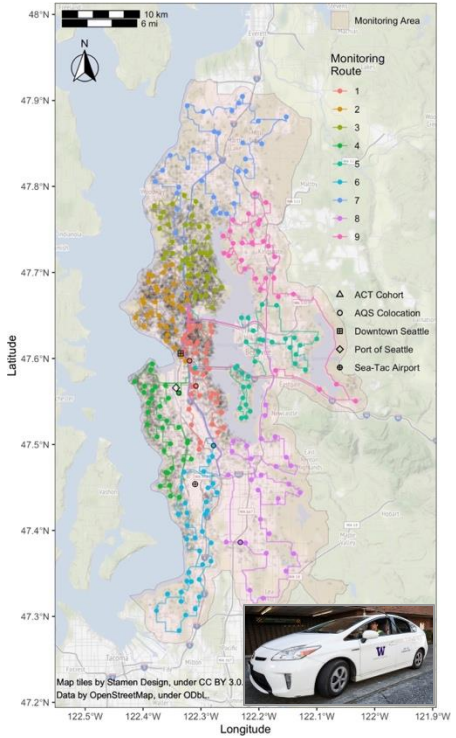
Ultrafine Particles (UFP)

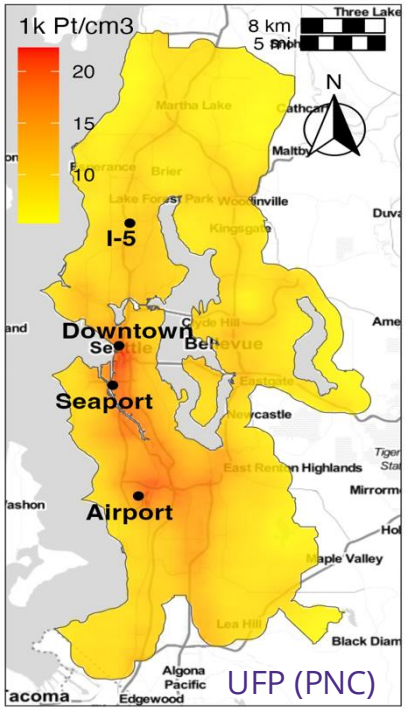


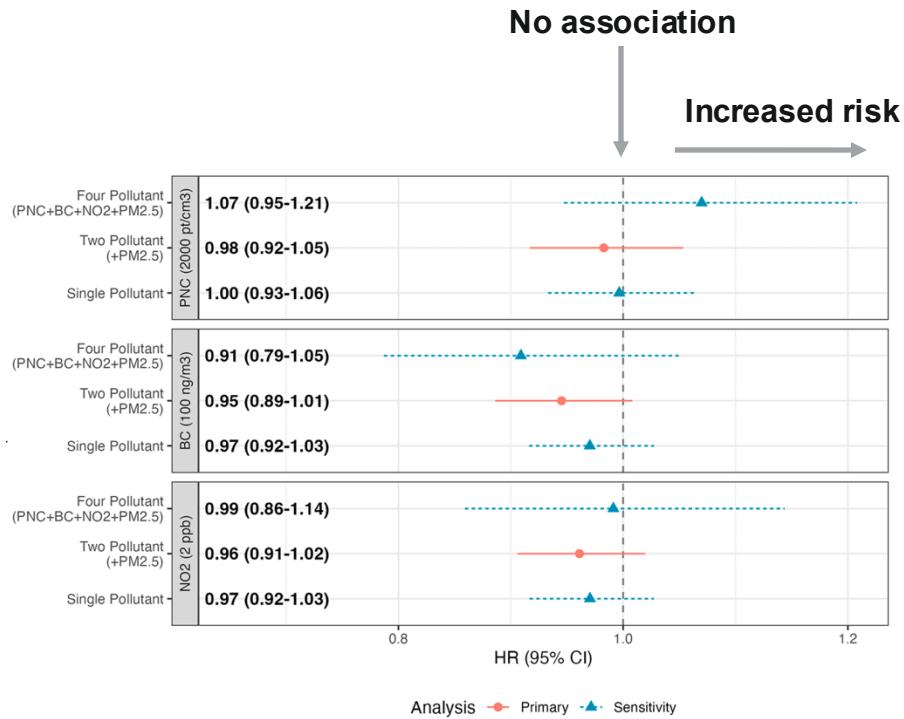


Left: https://now.tufts.edu/2018/09/20/toxic-air-we-breathe. **Right:** Kilian & Kitazawa 2018

UFP, Traffic Pollution, and Dementia in ACT



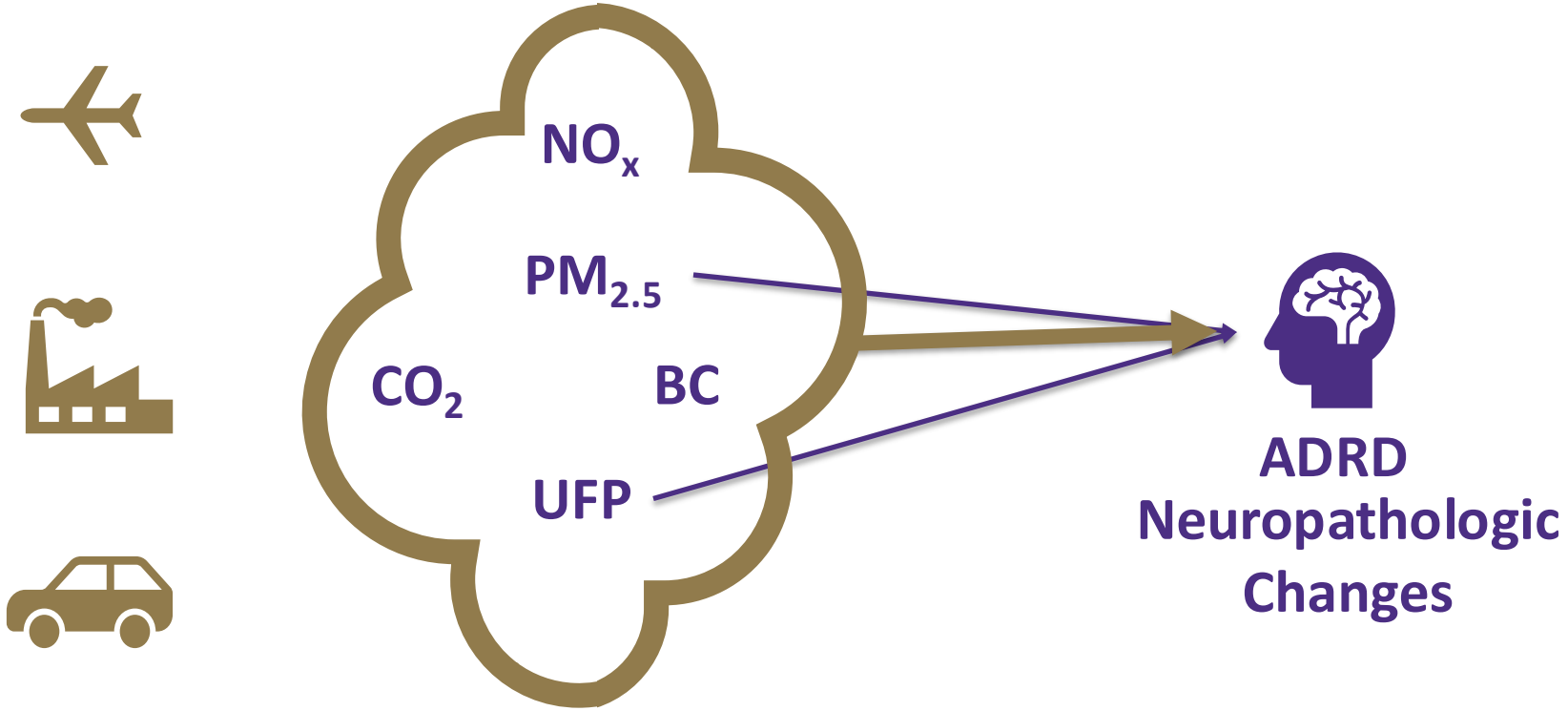




Blanco et al. 2022. ES&T. *Traffic pollution mobile monitoring campaign.* DOI: 10.1021/acs.est.2c01077

Blanco et al. 2024. Envt Int. *Traffic pollution and dementia in ACT*. DOI: 10.1016/j.envint.2024.108418

Air Pollution and ADRD



Something from nothing

Research Directions

CURRENT EVIDENCE	RESEARCH INTERESTS
Exposure to individual regulated pollutants	UFP & air pollution **mixtures**
Mostly clinical outcomes (e.g., dementia)	Mechanistic outcomes: **neuropathologic** changes
At-risk populations & highly selective autopsy samples	Inferences about the **general population** of older adults
Overall effects	Affected **subgroups**

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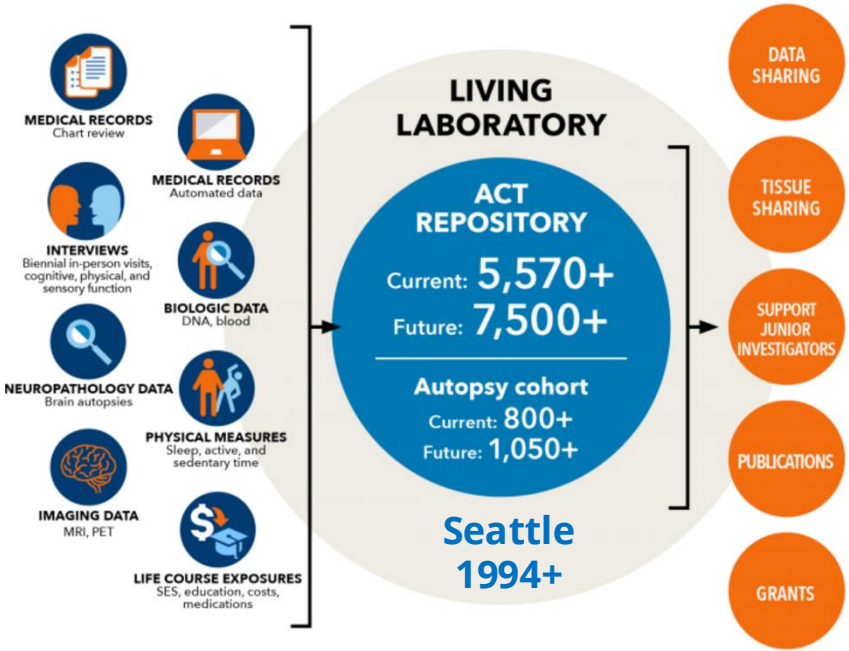
PLANNED WORK

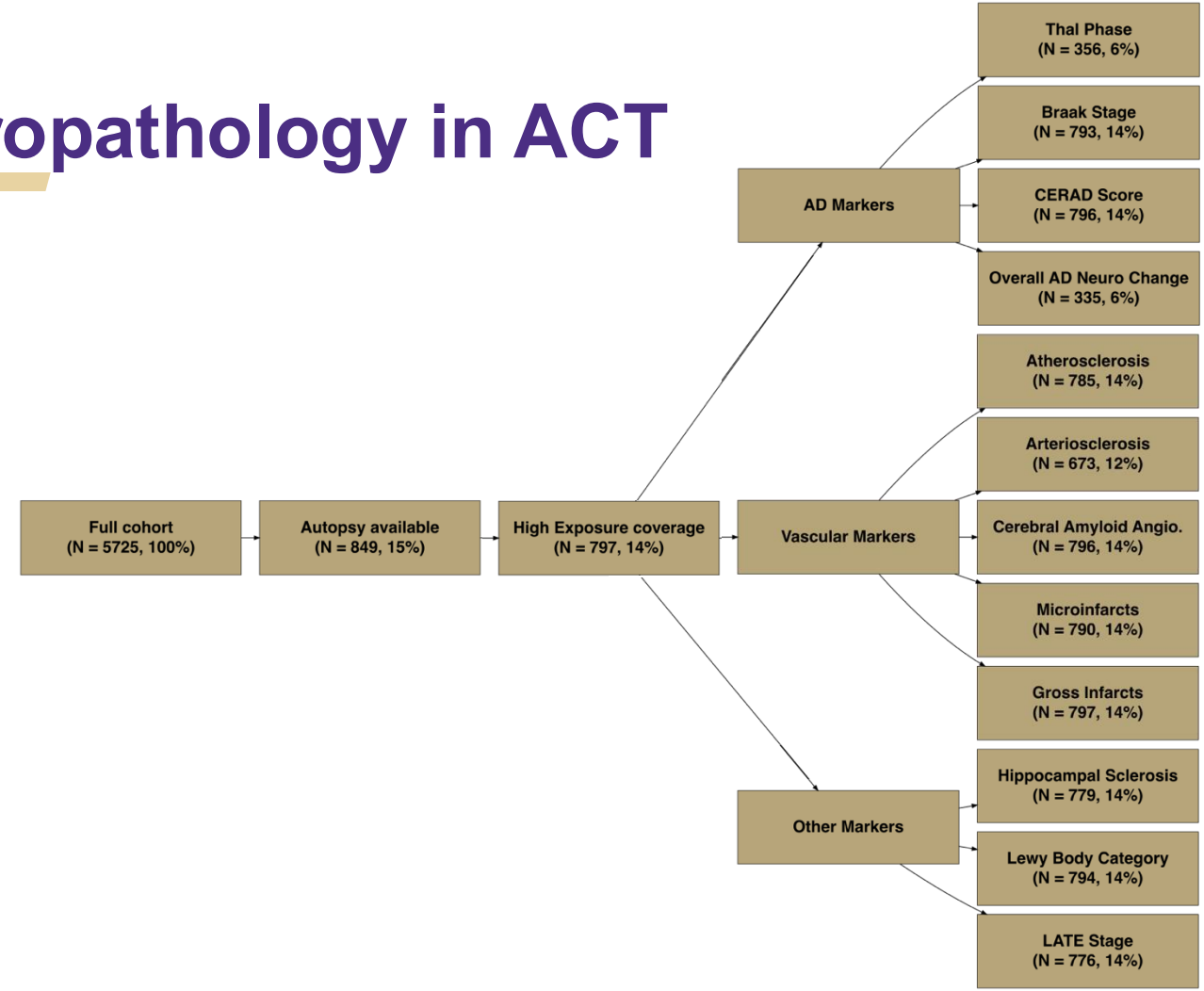
ACT Autopsy Cohort



ACT
ADULT CHANGES IN THOUGHT STUDY

KAISER PERMANENTE®
Kaiser Permanente Washington Health Research Institute

Neuropathology in ACT

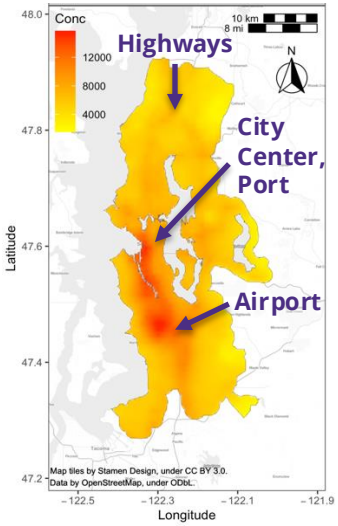


2020 Freeze

Air Pollution Exposure Assessment

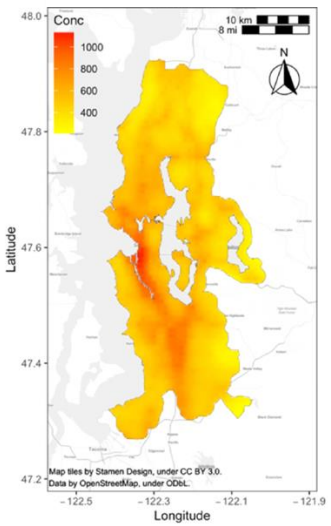
10y prior to autopsy

UFP (pt/cm³)

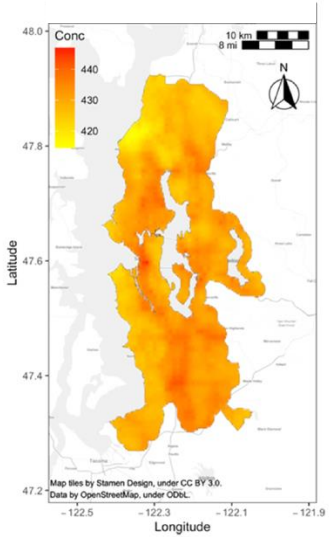


Blanco et al. 2022

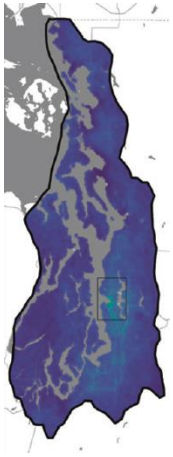
BC (ng/m³)



CO_2 (ppm)

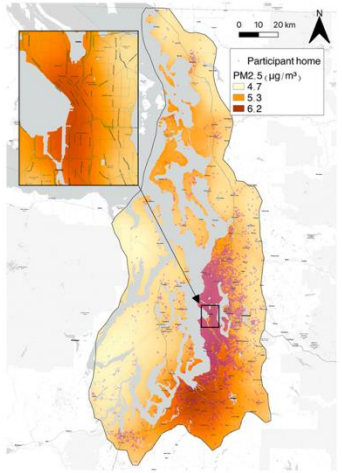


NO_x (ppb)



Zuidema et al. 2024

$PM_{2.5}$ (µg/m³)

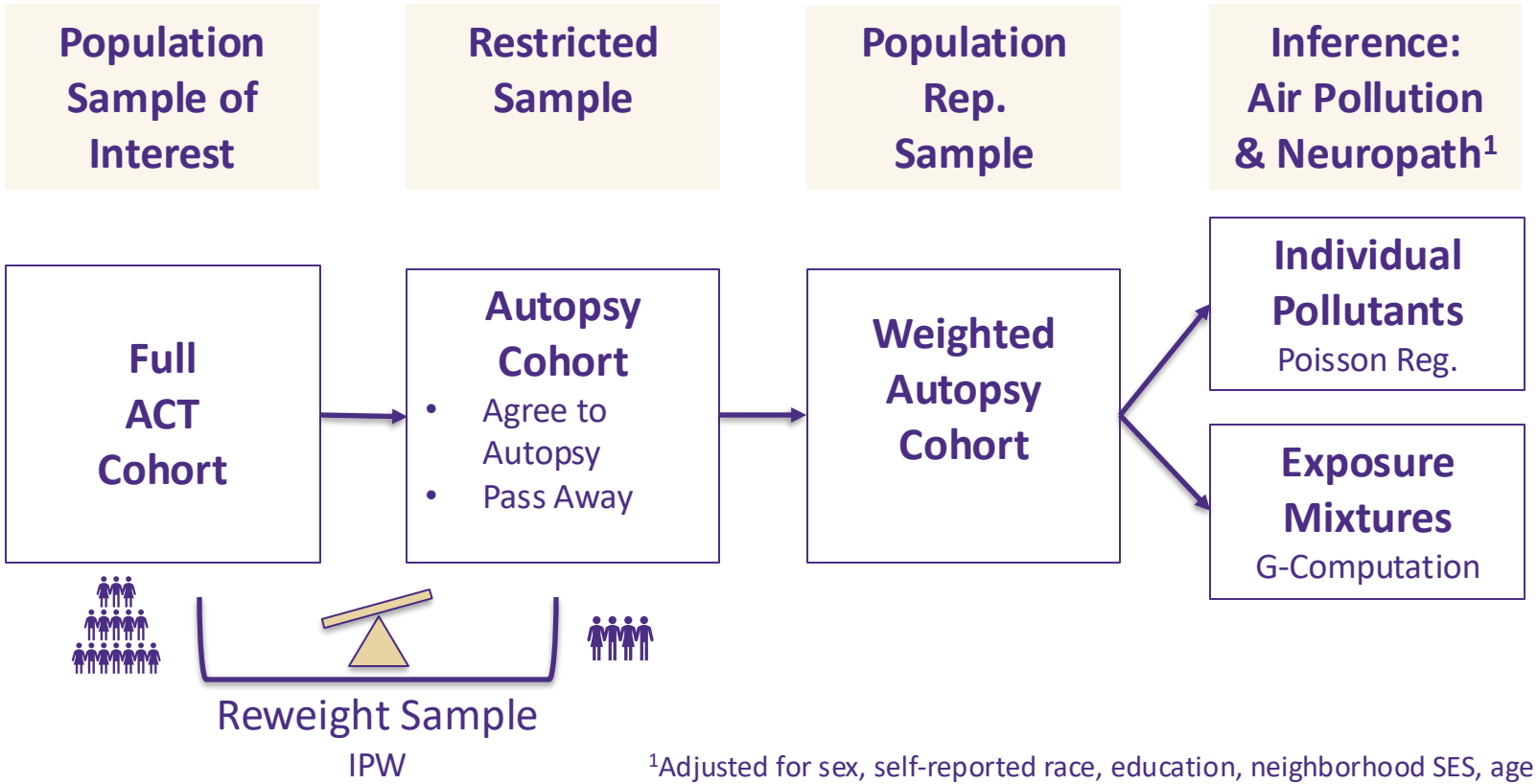


Shaffer et al. 2021

Mobile Monitoring (2019-2020)

Fixed & Temporary Sites

Analytic Overview



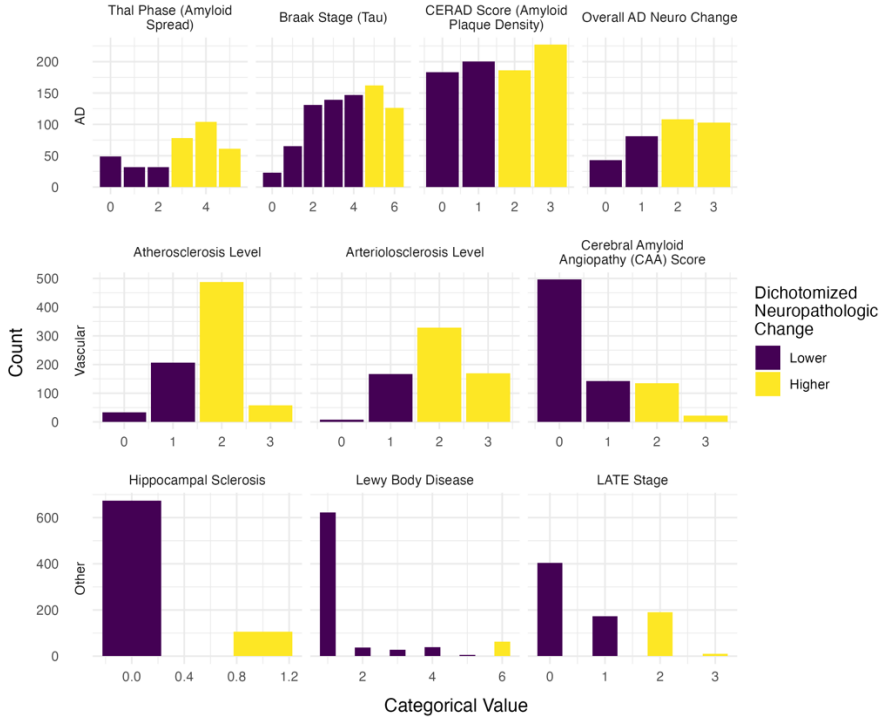
[1]Adjusted for sex, self-reported race, education, neighborhood SES, age at death, year

Results

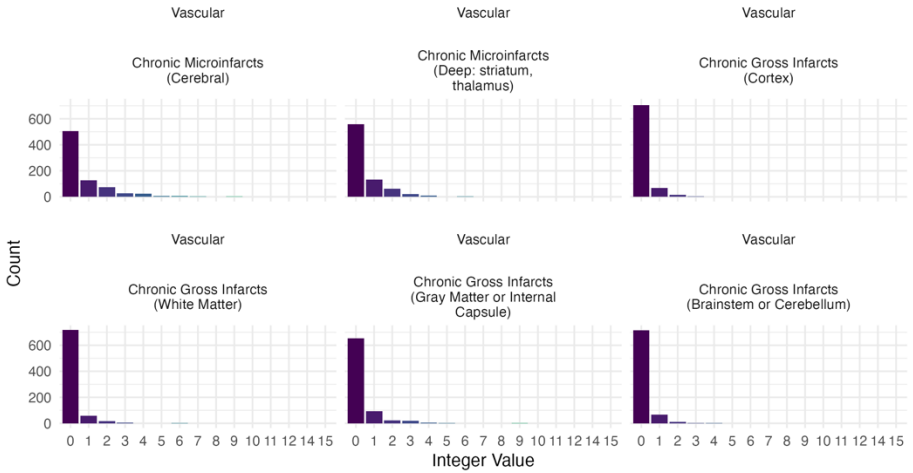
Cohort Characteristics

	Autopsy Cohort (N=797)	Original Cohort (N=5725)
Age at Death		
Mean (SD)	89.1 (6.7)	87.7 (7.1)
Missing	0 (0%)	2341 (40.9%)
Sex		
Female	457 (57%)	3320 (58%)
Male	340 (43%)	2405 (42%)
Race		
White	750 (94%)	5119 (89%)
People of Color	47 (6%)	606 (11%)
Education		
None	62 (8%)	461 (8%)
GED or HS	332 (42%)	2104 (37%)
Bachelor's	189 (24%)	1356 (24%)
Master's	109 (14%)	916 (16%)
Doctorate	45 (6%)	343 (6%)
Other	60 (8%)	545 (10%)
Neighborhood SES		
Mean (SD)	-0.7 (0.7)	-0.7 (0.7)
Year of Death		
Mean (SD)	2010.2 (6.0)	2009.1 (6.9)
Missing	0 (0%)	2341 (40.9%)

Neuropathology Measures at Autopsy

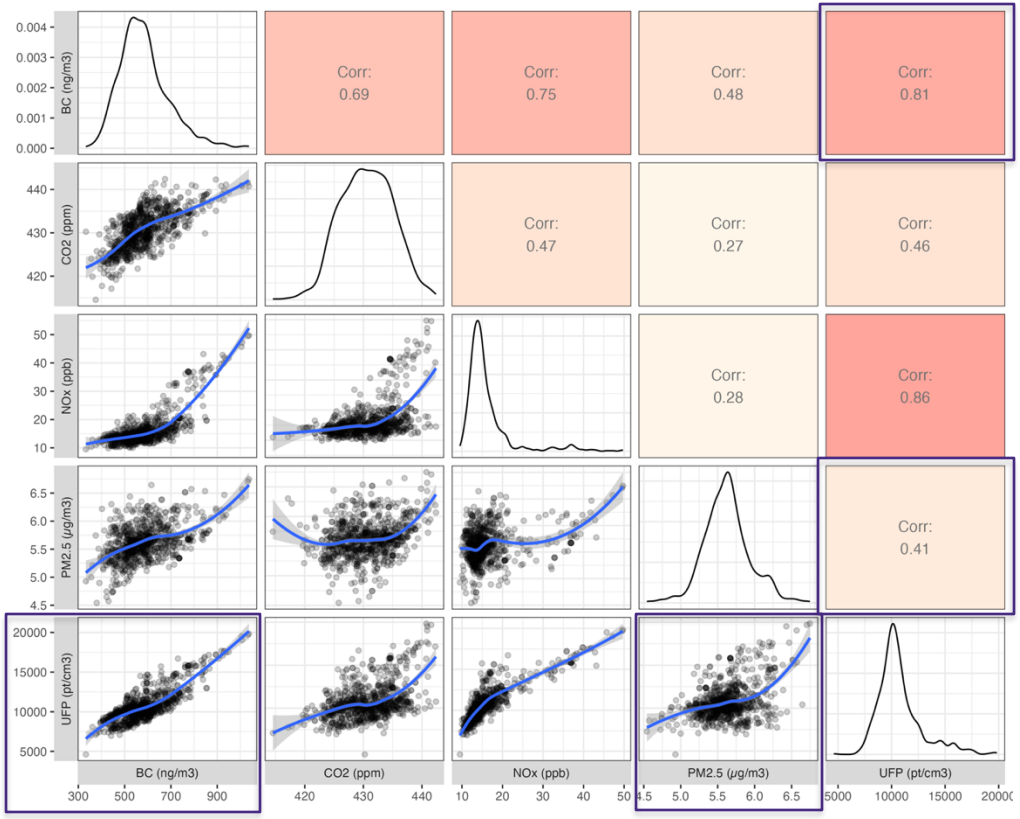


Transformed to dichotomous outcomes

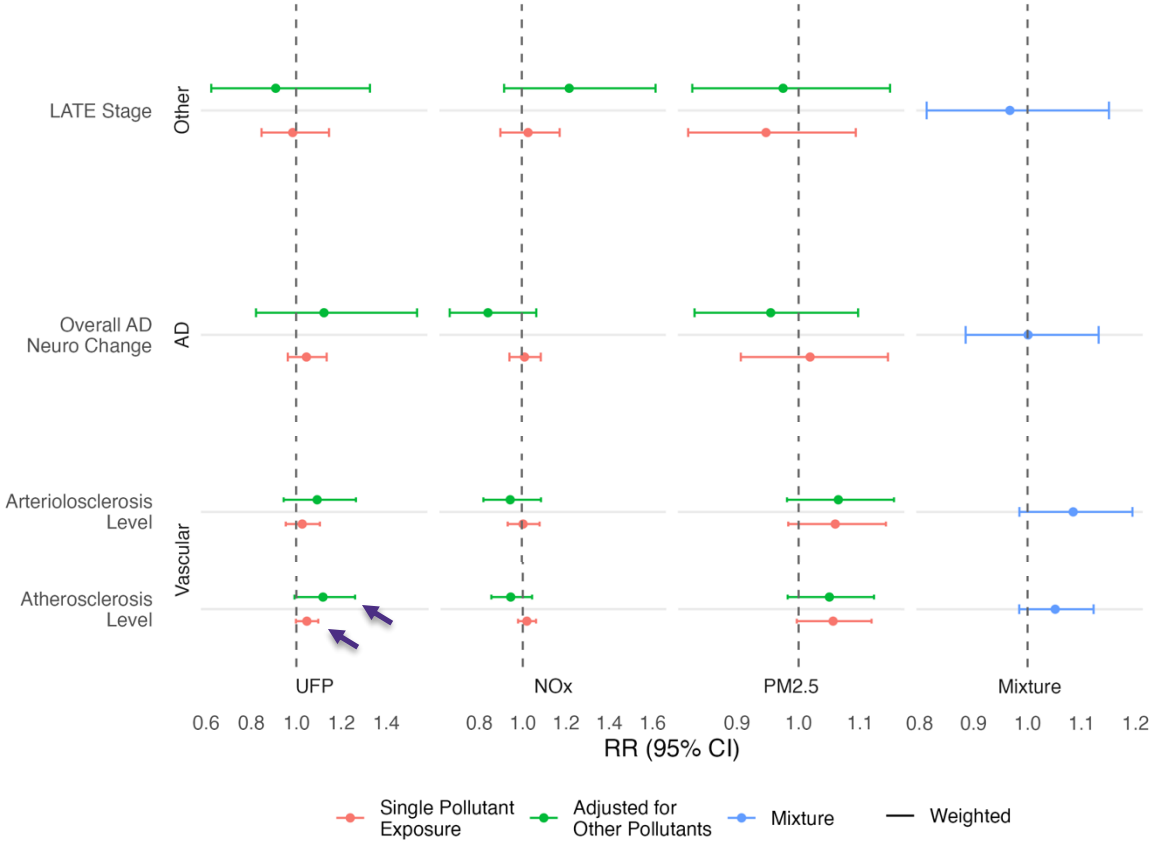


Count outcomes

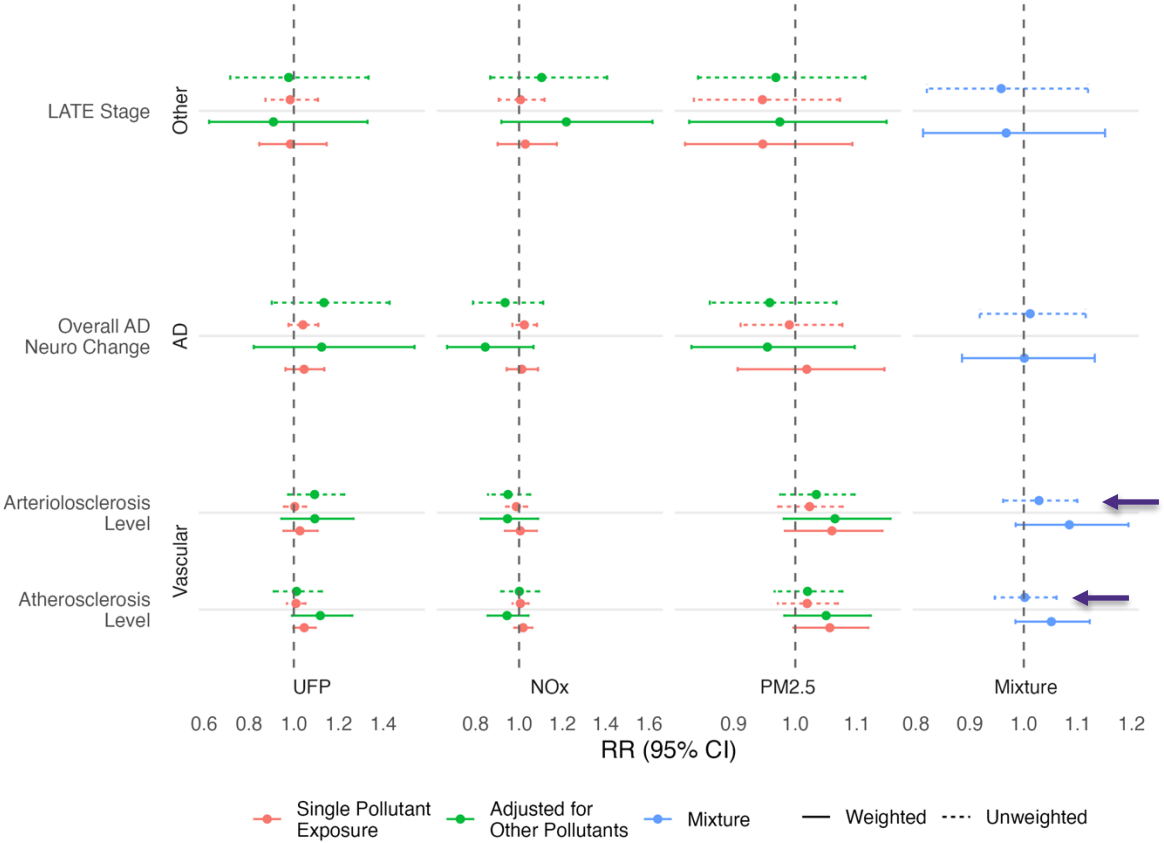
Predicted Exposures (10 Years Prior to Autopsy)



Relative Risk of Elevated Neuropathology per SD Increase in Pollutant Conc.



Relative Risk of Elevated Neuropathology per SD Increase in Pollutant Conc.



Attenuated Estimates

Agenda

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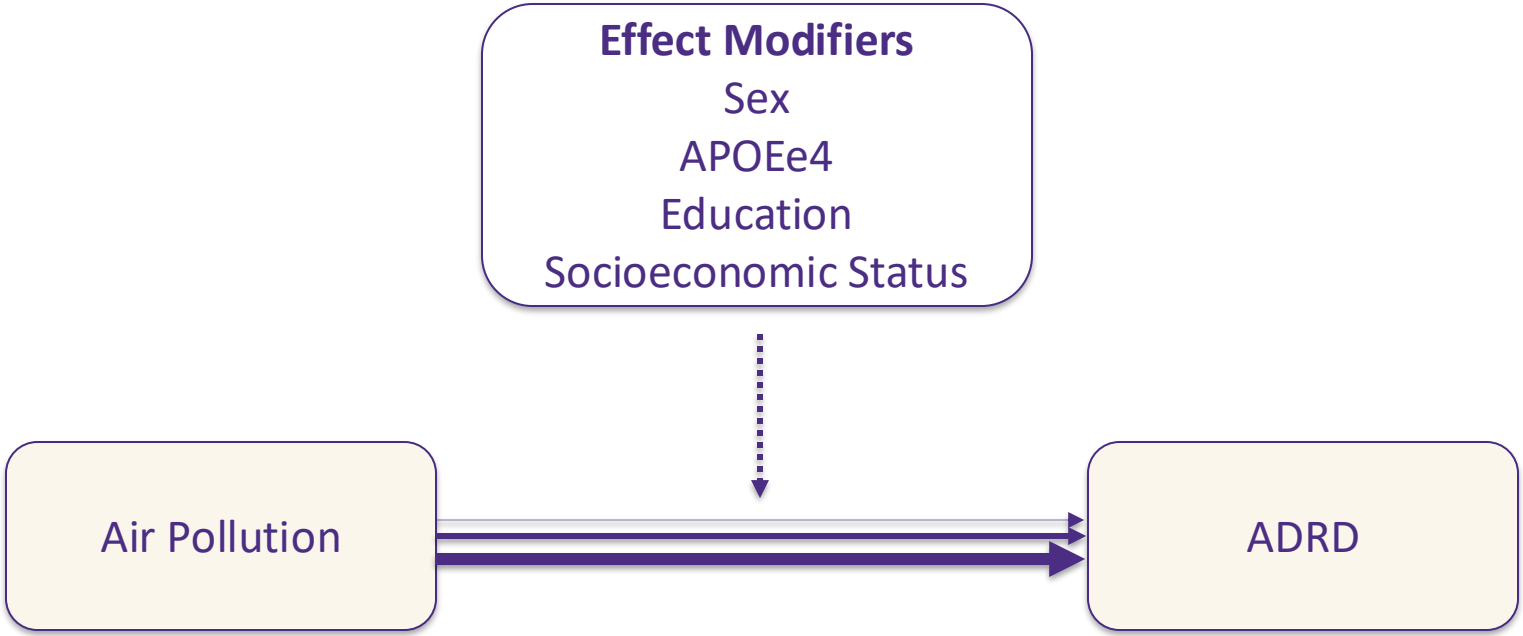
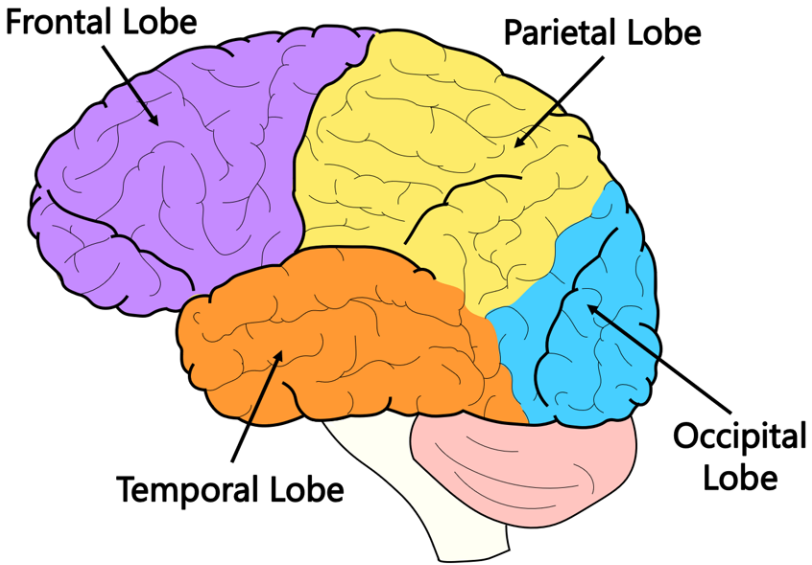
PLANNED WORK

Heterogeneity by Demographic and Genetic Factors



*Simplified Diagram

Quantitative Neuropathology by Brain Region



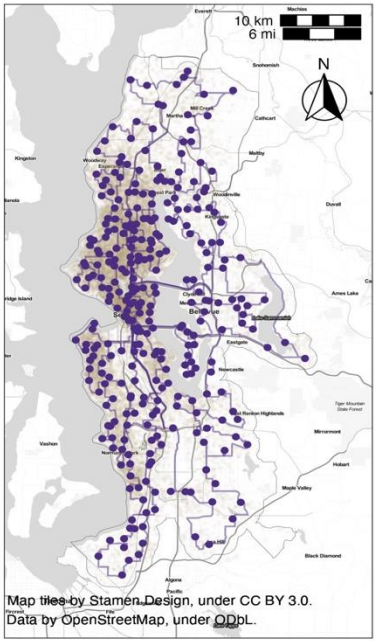
Aβ40, Aβ42

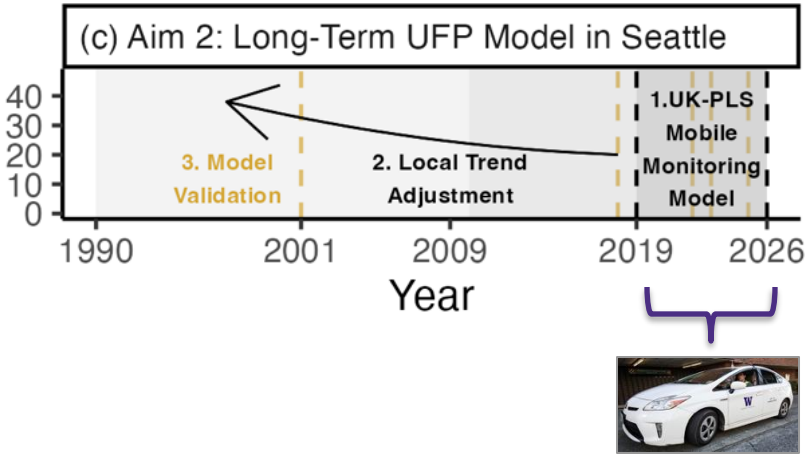
Phospho-tau (p-tau)

Phospho-TDP-43 (pTDP-43)

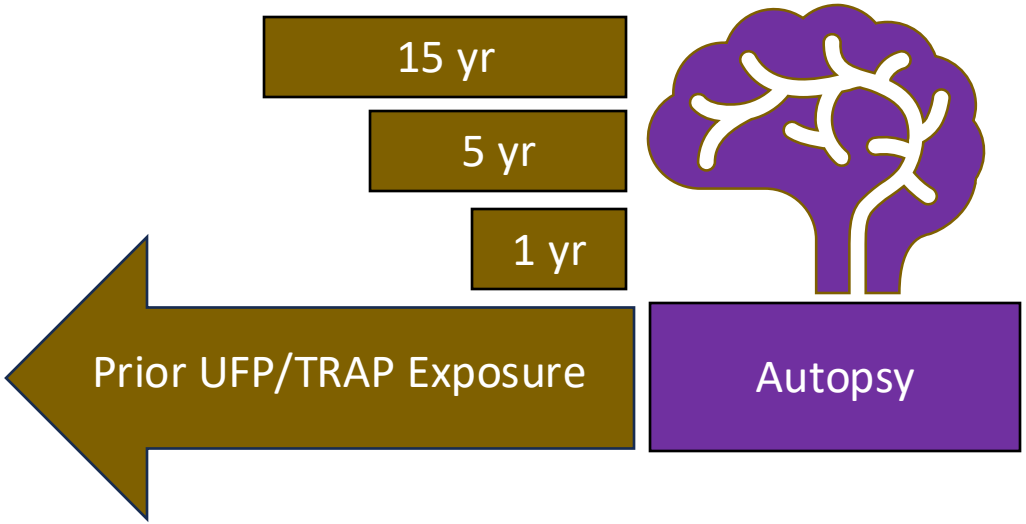
Image: https://www.brainframe-kids.com/brain/facts-lobes.htm

Long-Term UFP Models





Critical Exposure Windows



Thank You!

ACT PARTICIPANTS

MENTORS: Drs. Lianne Sheppard, Paul Crane, Adam A. Szpiro, Caitlin Iatimer, Dirk Keene, Jennifer Weuve, Marco Carone

RESEARCH COLLABORATORS: Drs. Helen Suh Lab, PhD Trent Honda, Joshua Sonnen

STAFF SUPPORT: Amanda Gassett, Brian High, KatieRose Johnson, Connie Nakano, And Many More!

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Magali Blanco, PhD

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Appendix

Who is Autopsied?

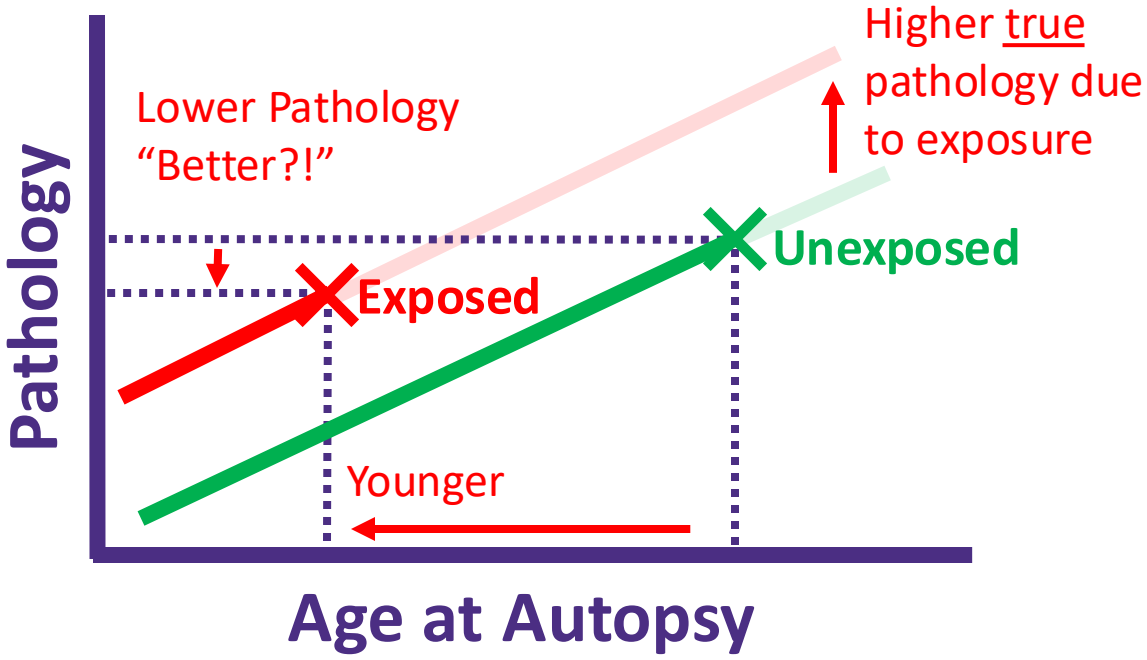
More likely to agree to autopsy

- Non-Hispanic White
- Dementia diagnosis
- CV Disease
- Smoking history
- No depression

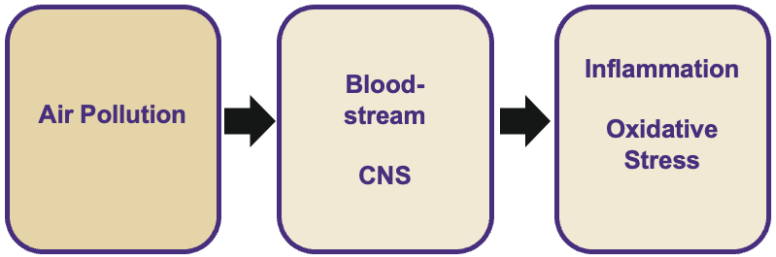
….and pass away

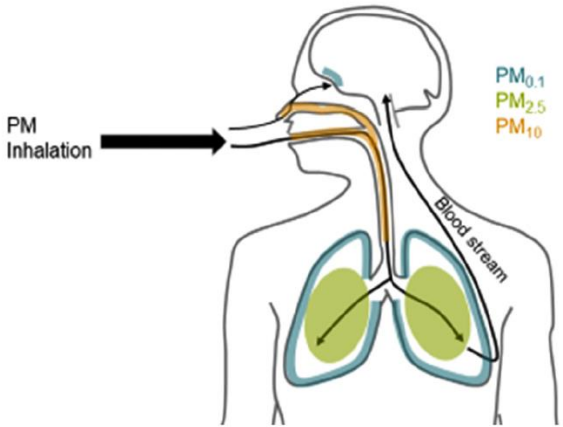
- Diabetes
- Alcohol problems
- Difficulty with ADL

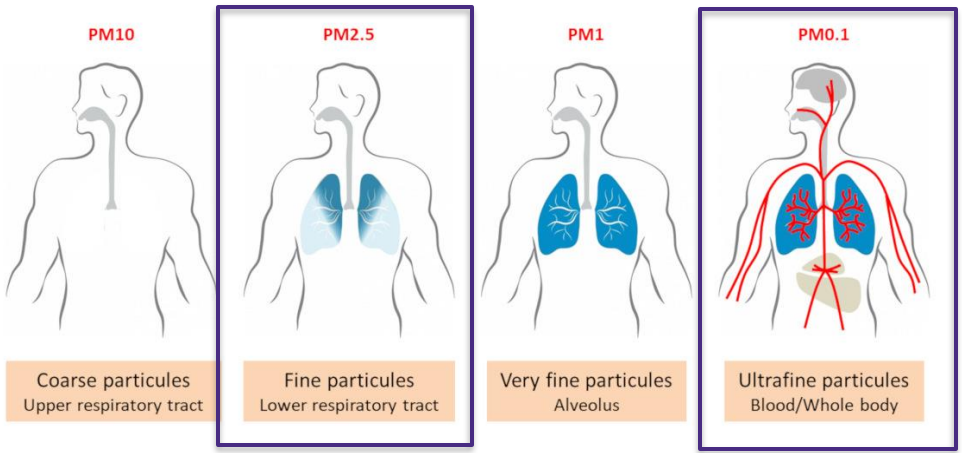
Survival Bias



Air Pollution and Aging Health







Left: Kilian & Kitazawa 2018. Right: https://www.encyclopedie-environnement.org/en/health/airborne-particulate-health-effects/

Air Pollution and Aging Health