# Some dirt might hurt

## *why the* **environment** *merits attention as a contributor to* **dementia risk**

JENNIFER WEUVE, MPH, SCD

MAY 2025

BOSTON UNIVERSITY SCHOOL of Public Health

# “Environmental exposure”

- Contact with a **chemical, biological**, or **physical** entity,
- found in the **air, water, soil, food, consumer products**, or **“sensory-scape,”**
- that may affect human **health**

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# “Environmental exposure”





persistent organic pollutants

**PCBs, PFAS, dioxins, DDT**


heavy metals

**Pb** **Cd** **As** **Hg**

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# **Why** should environmental exposures **merit our attention** for understanding dementia risk?

4 INTERCONNECTED REASONS …

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1. **Exposures to *known neurotoxicants*, are or were *common* among children and middle-aged adults.**

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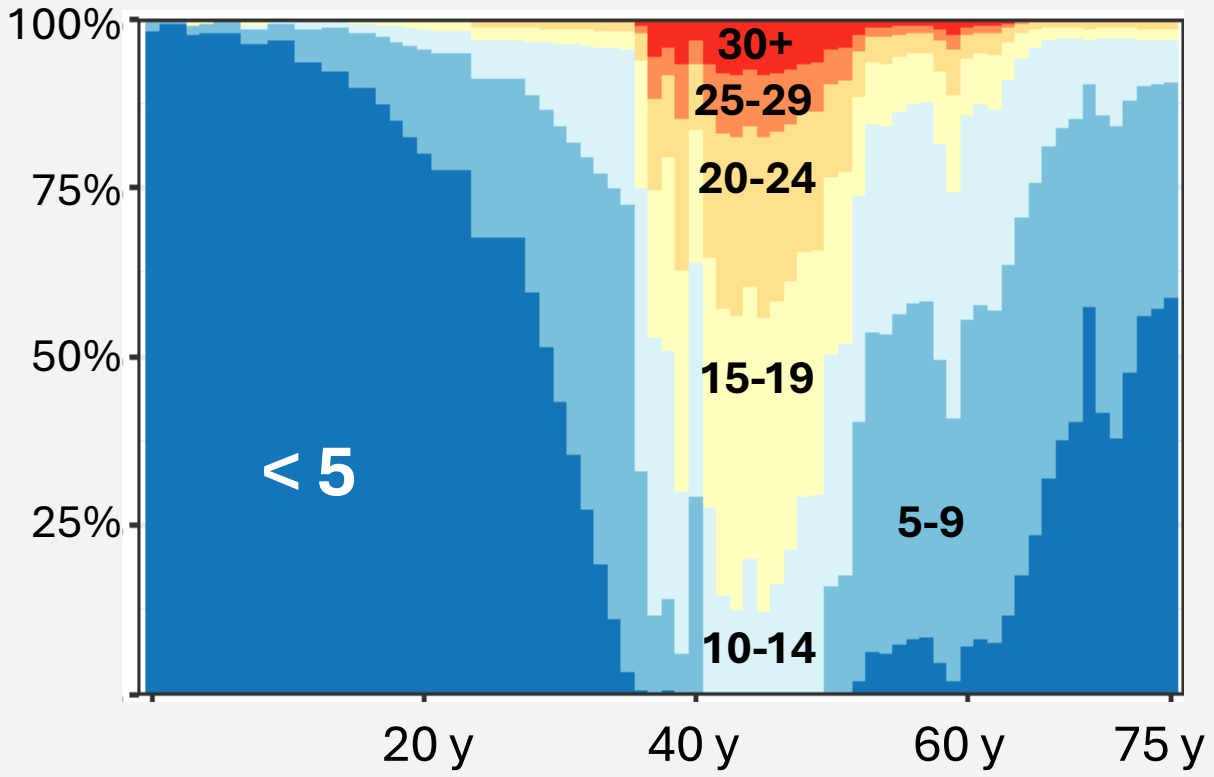
% of US population, **by age**, who had given **childhood blood LEAD level, µg/dL** (2015)




McFarland, et al. Proc Natl Acad Sci U S A. 2022;119(11). PMC8931364.

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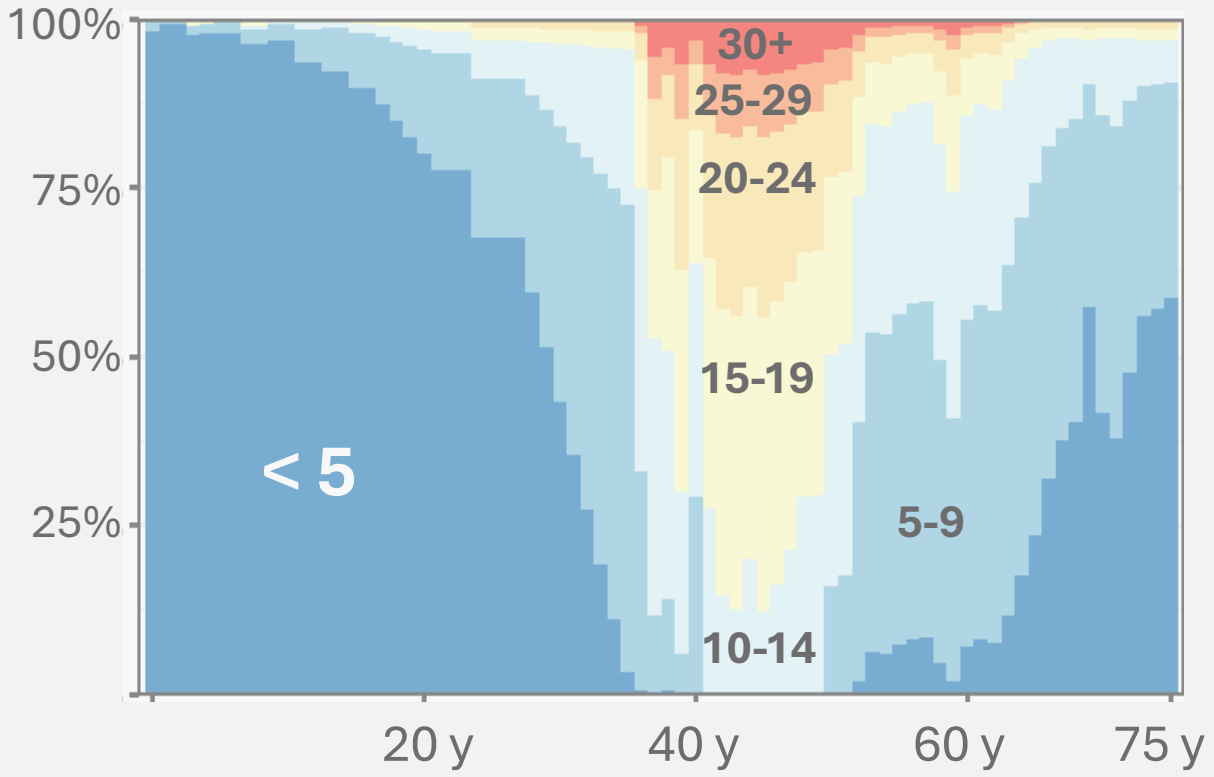


McFarland, et al. Proc Natl Acad Sci U S A. 2022;119(11). PMC8931364.

## PESTICIDES

**Most children** exposed at home

**1.8 billion agricultural workers** globally

50 million US residents use **contaminated groundwater**

Alavanja MC. Rev Environ Health. 2009:24(4). PMC2946087.

U.S. Dept of Veterans Affairs. Exposure Related Health Concerns. https://www.publichealth.va.gov/exposures/health-concerns.asp

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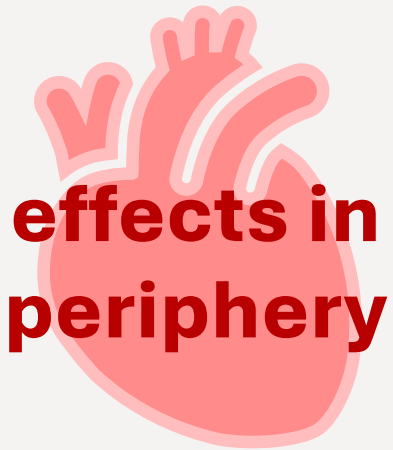
## 2. Some exposures may act *pleiotropically* in affecting dementia etiology.


dementia

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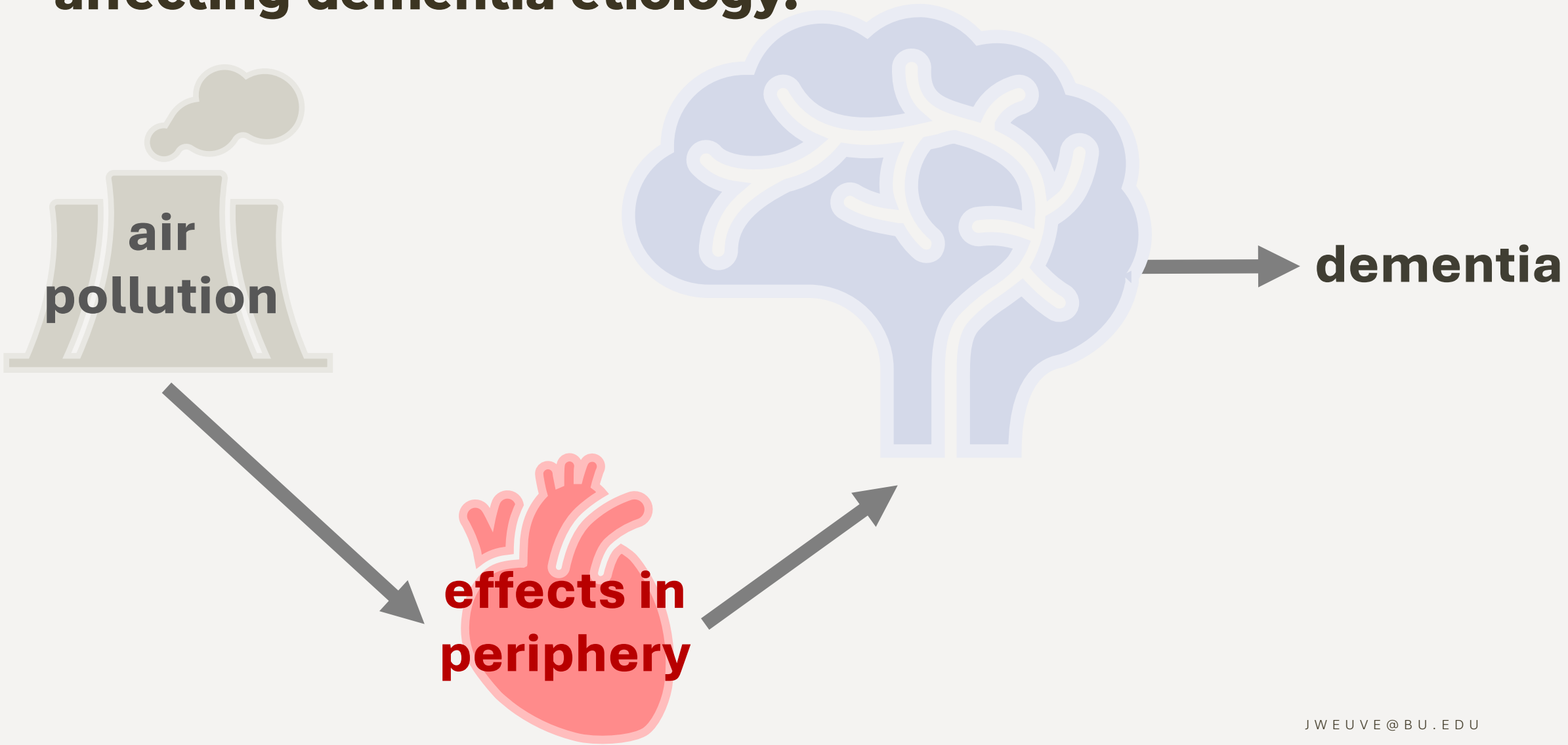


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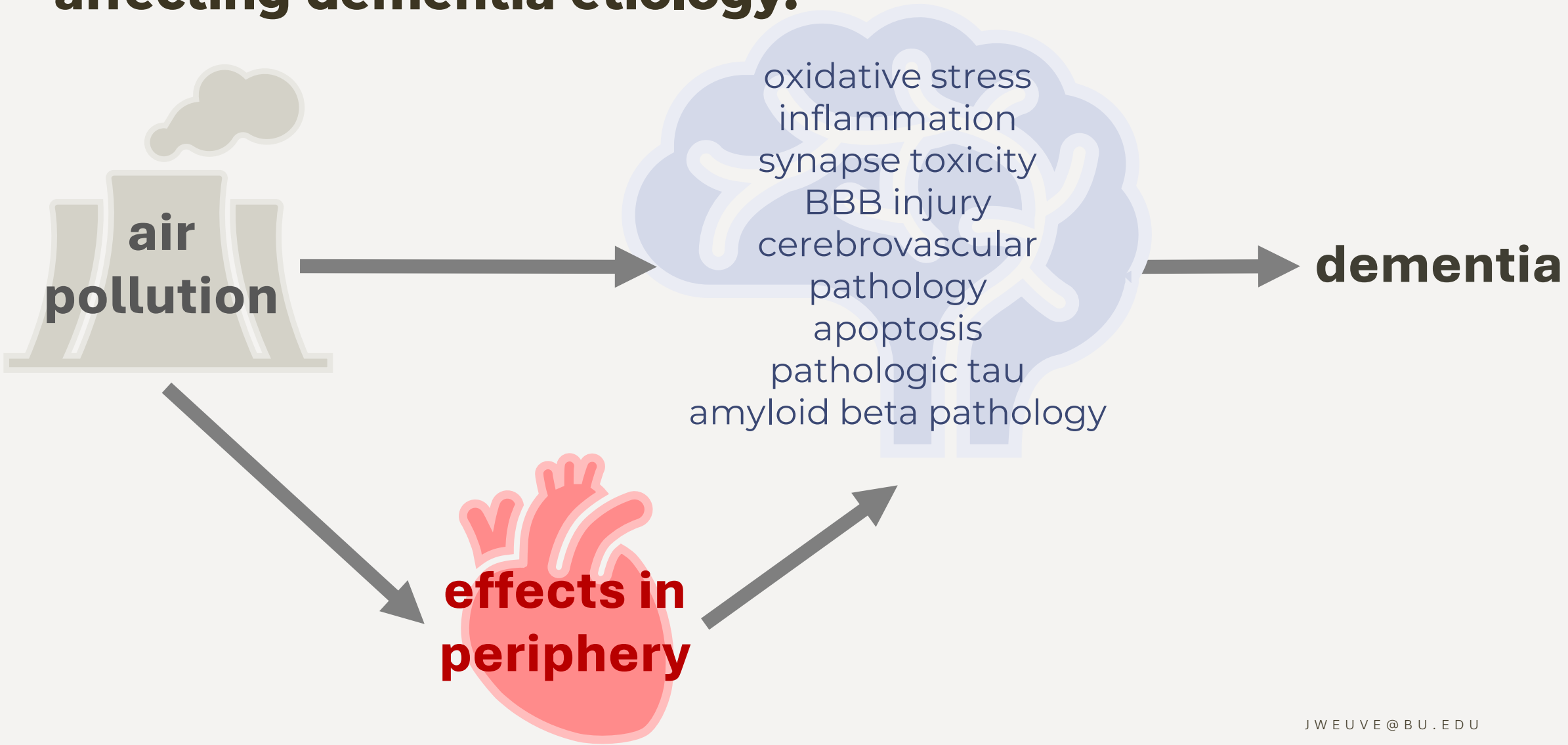


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Geometric mean blood lead concentration among 1- to 5-year-old children in the US, µg/dL



Year

Egan et al. Environ Health Perspect. 2021;129(3). PMC7969125.

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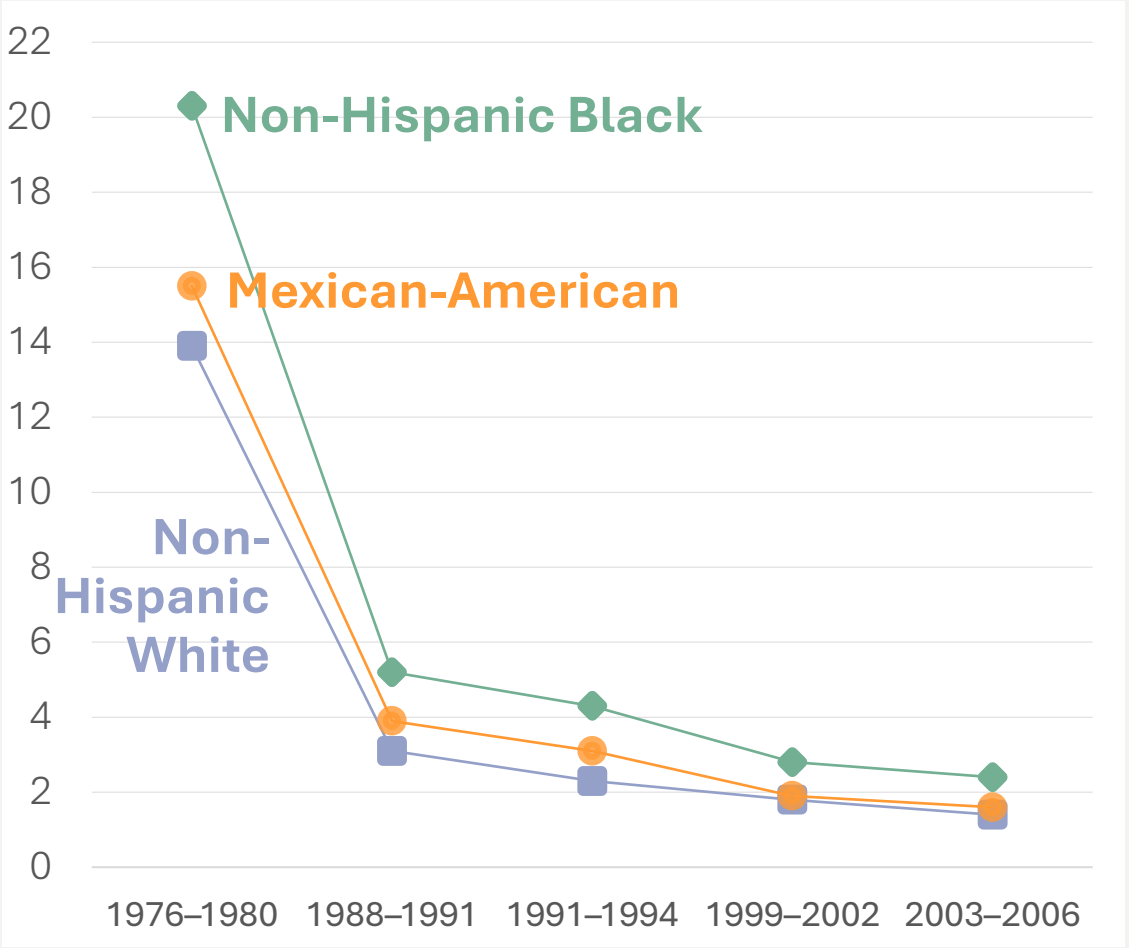


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# 4. *Untapped potential* for large impact on the public health burden of dementia.

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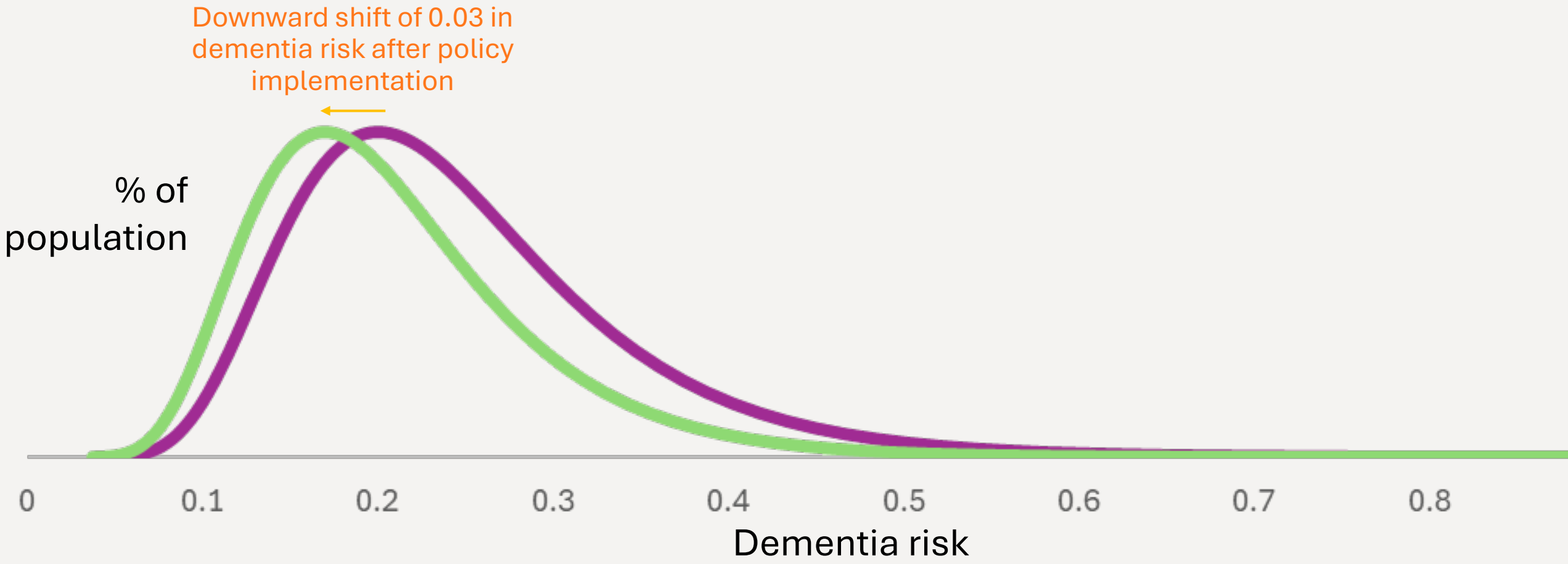
Grosse et al. Env Health Perspect. 2002. PMC1240871

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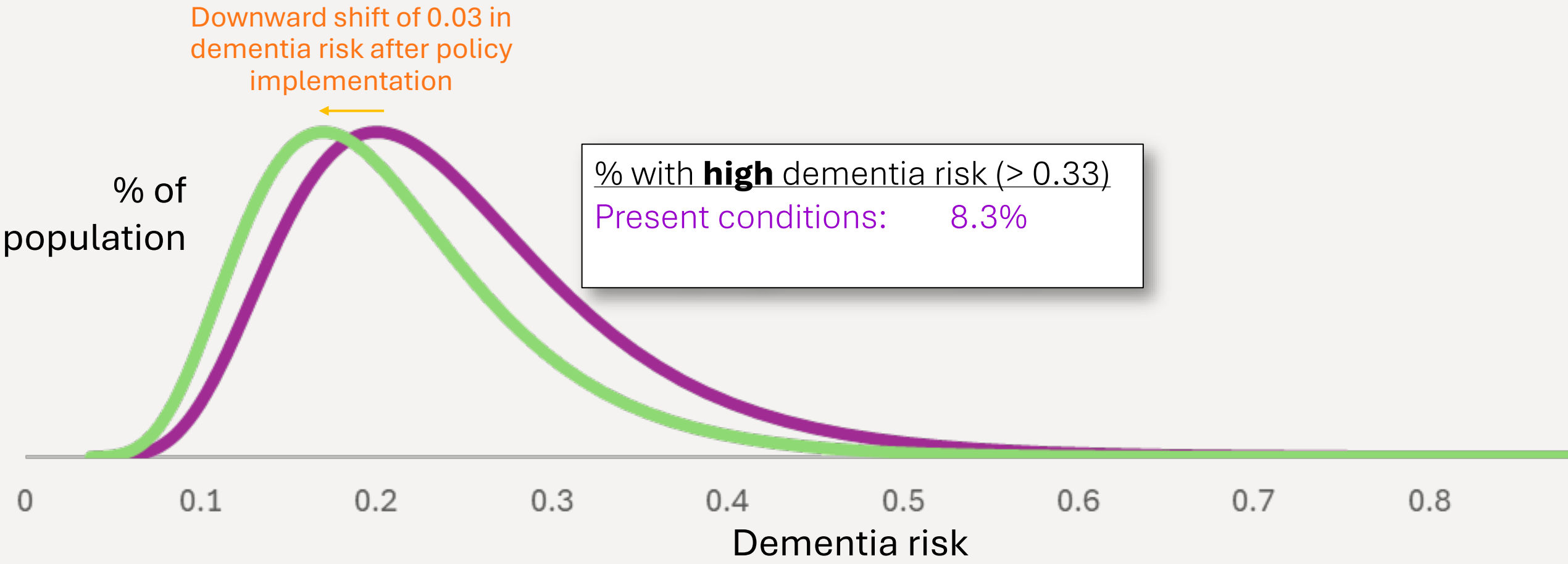


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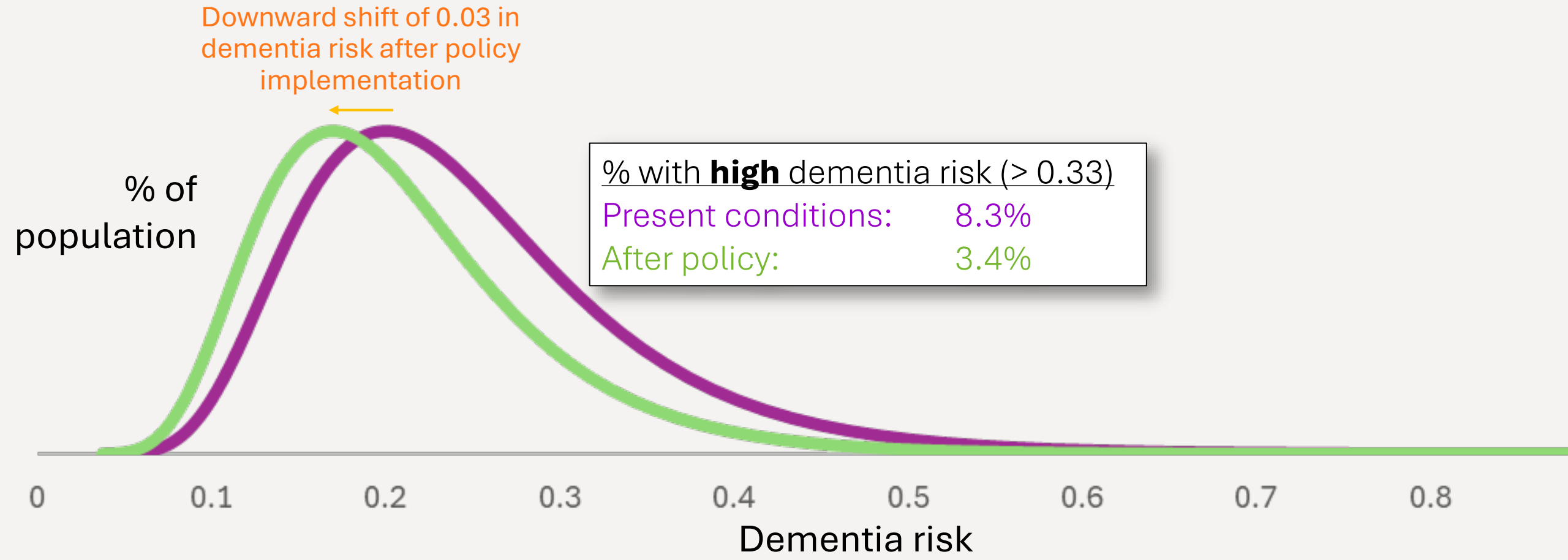


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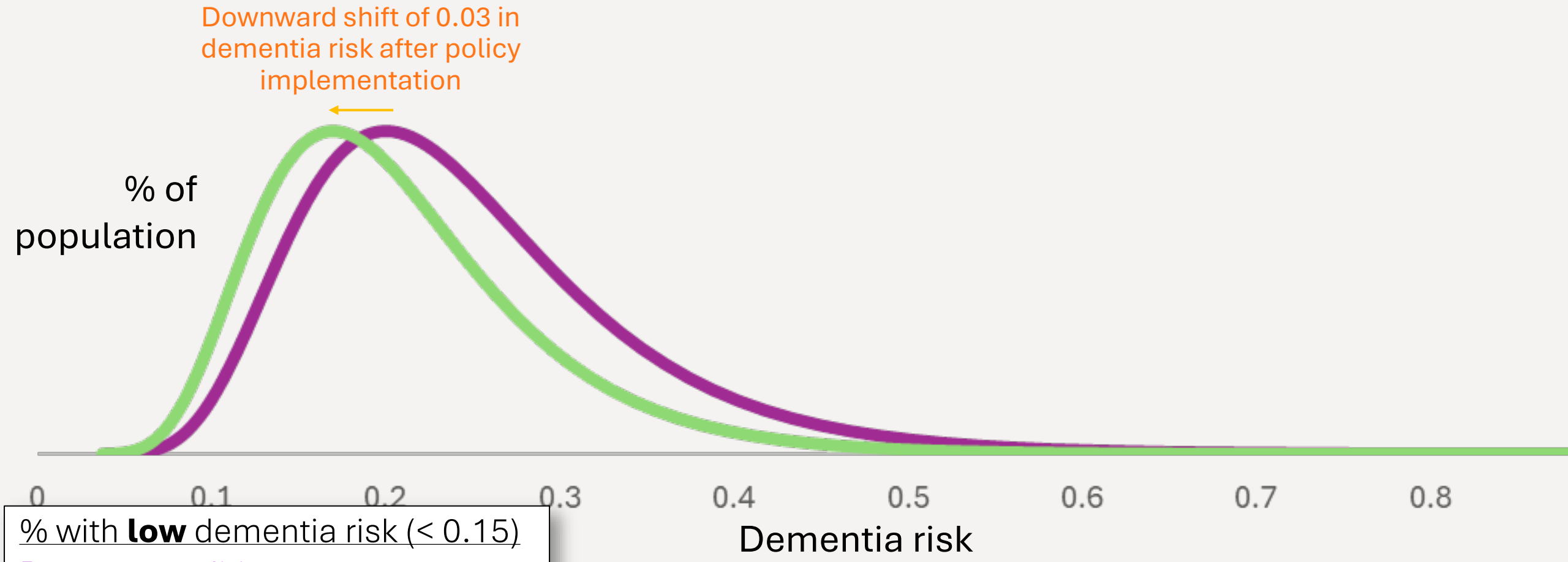


% with **low** dementia risk (< 0.15)

Present conditions: 22%

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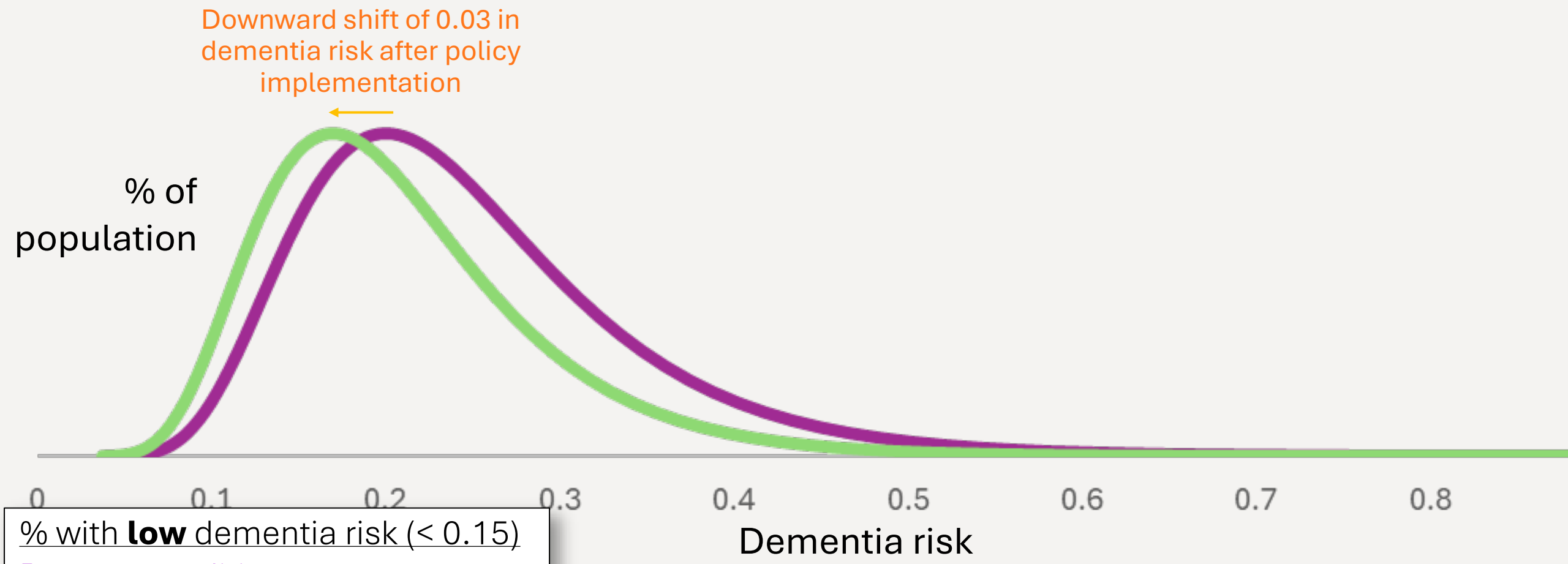


| % with **low** dementia risk (< 0.15) | |
|---|---|
| Present conditions: | 22% |
| After policy: | 37% |

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# 2 environmental exposures in relation to dementia risk

EVIDENCE FROM THE FIELD

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# AIR POLLUTION:

**Contaminants** in outdoor air

from **burning** and **grinding**

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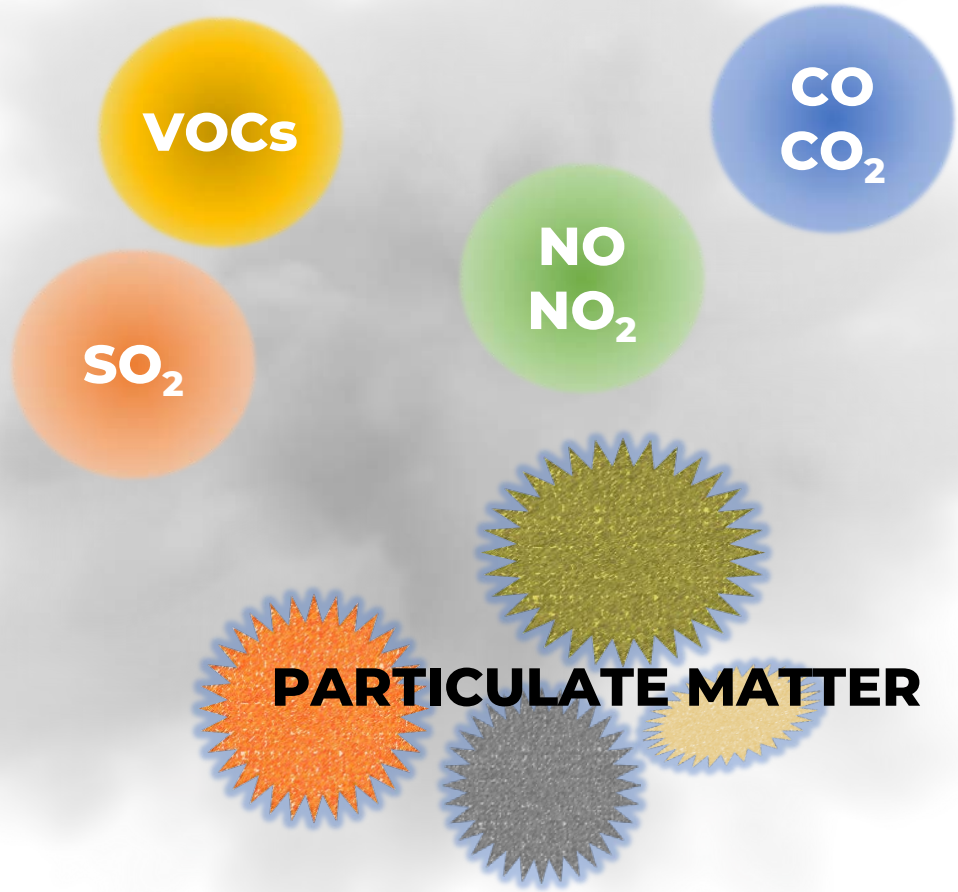
# PRIMARY

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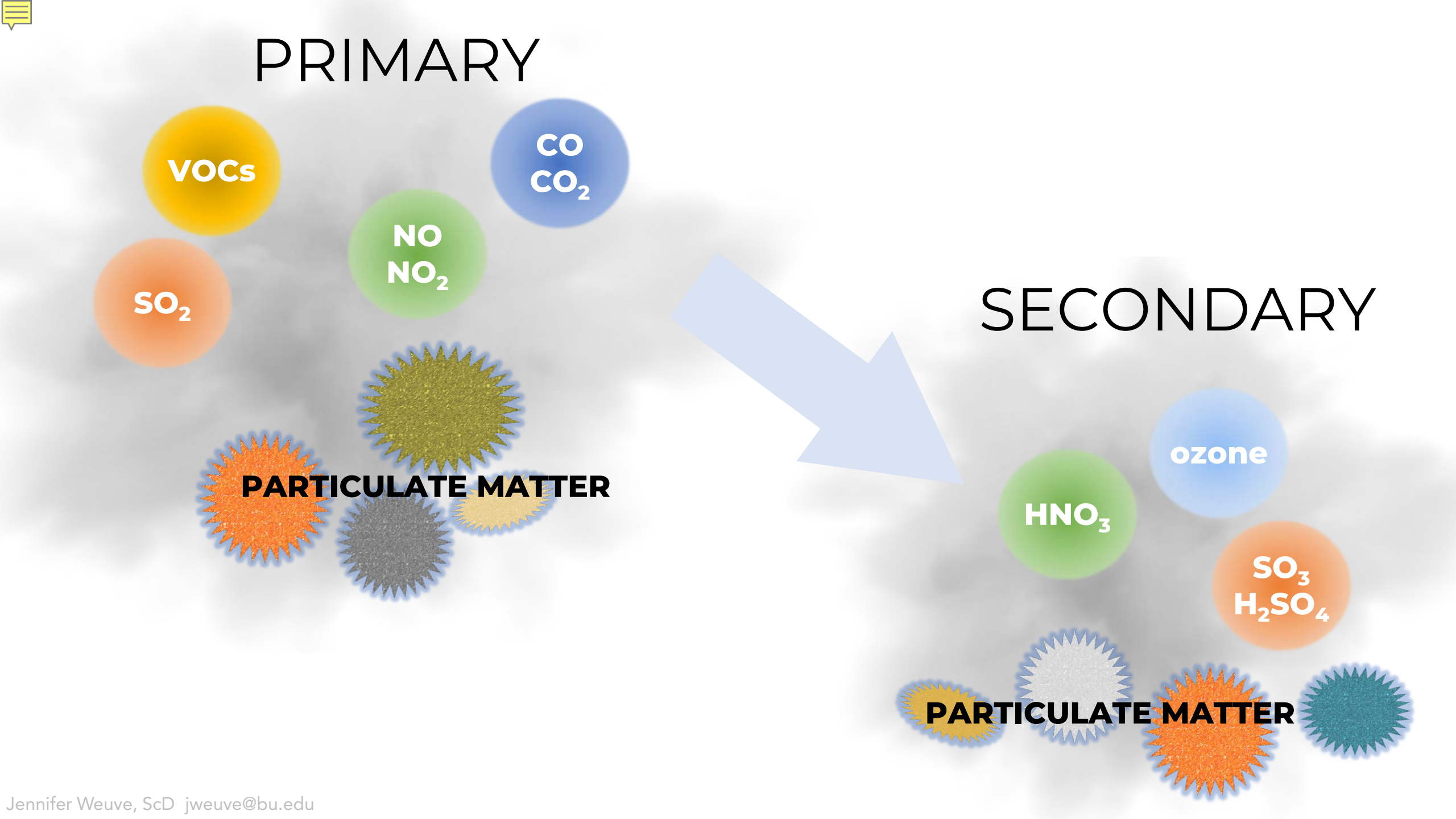


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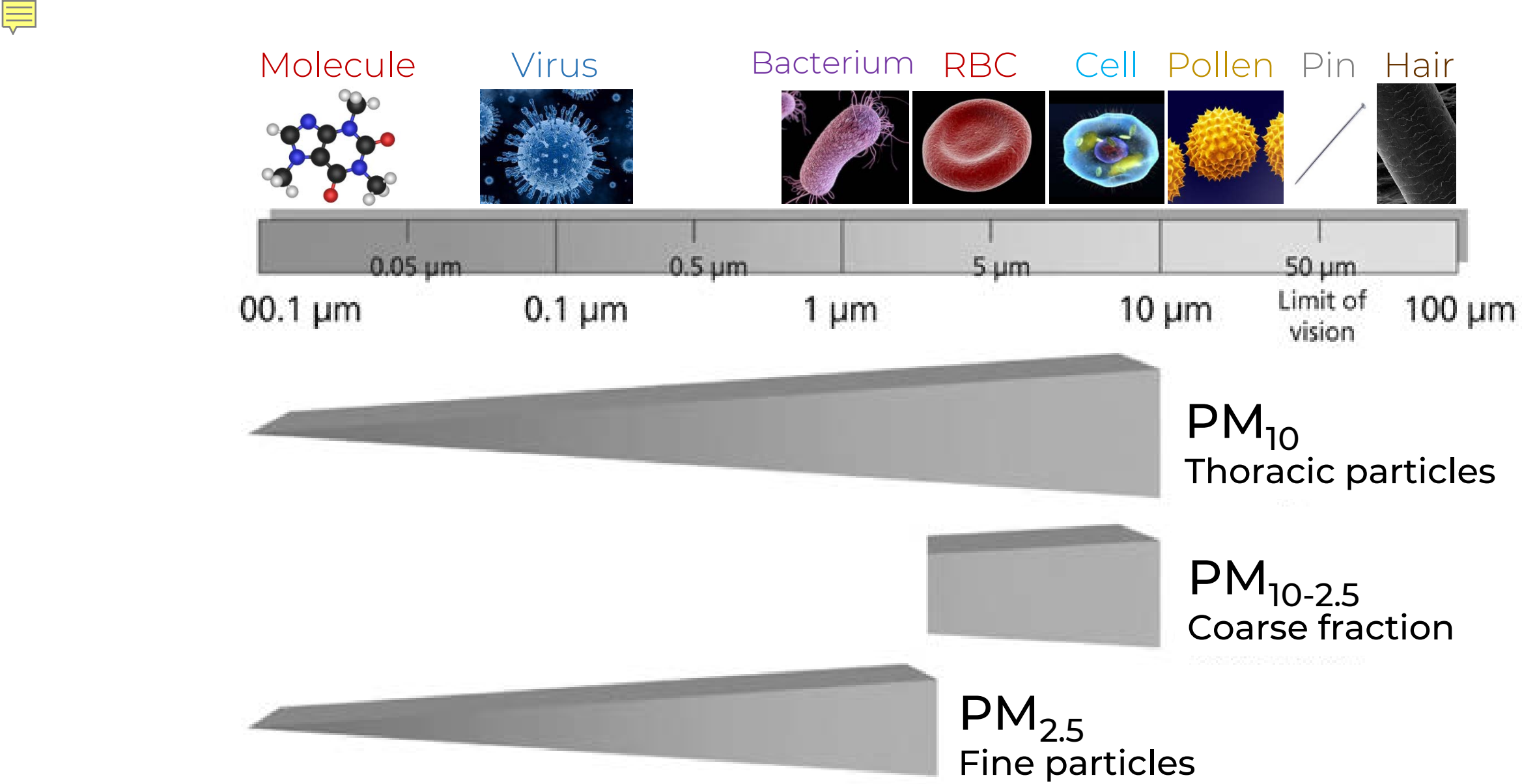
Molecule
Virus
Bacterium
RBC
Cell
Pollen
Pin
Hair
0.05 µm
0.5 µm
5 µm
50 µm
00.1 µm
0.1 µm
1 µm
10 µm
Limit of vision
100 µm
PM10
Thoracic particles
PM10-2.5
Coarse fraction
PM2.5
Fine particles

# How might exposure to air pollution influence dementia etiology?

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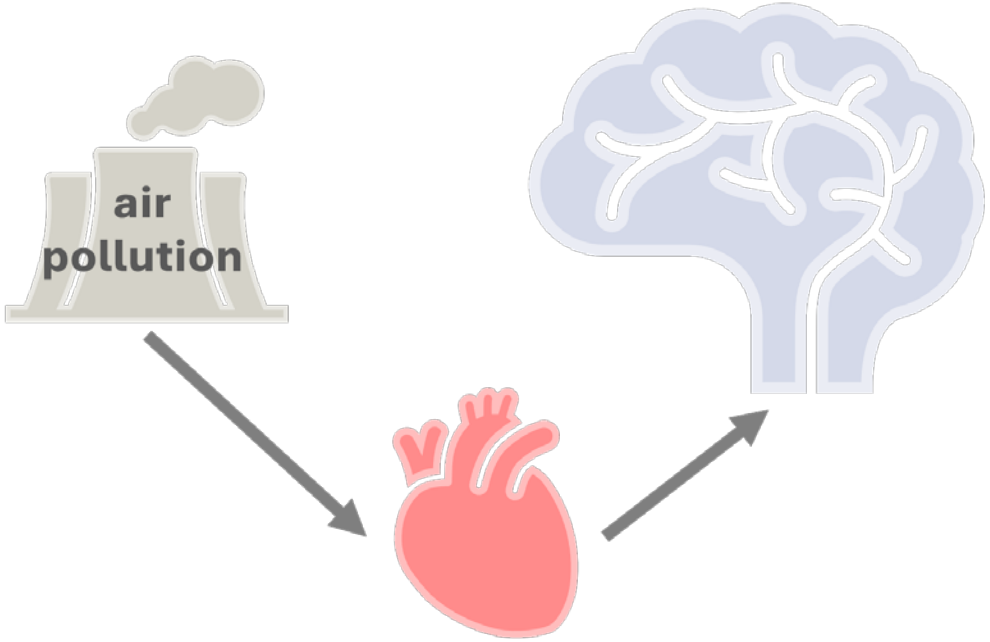


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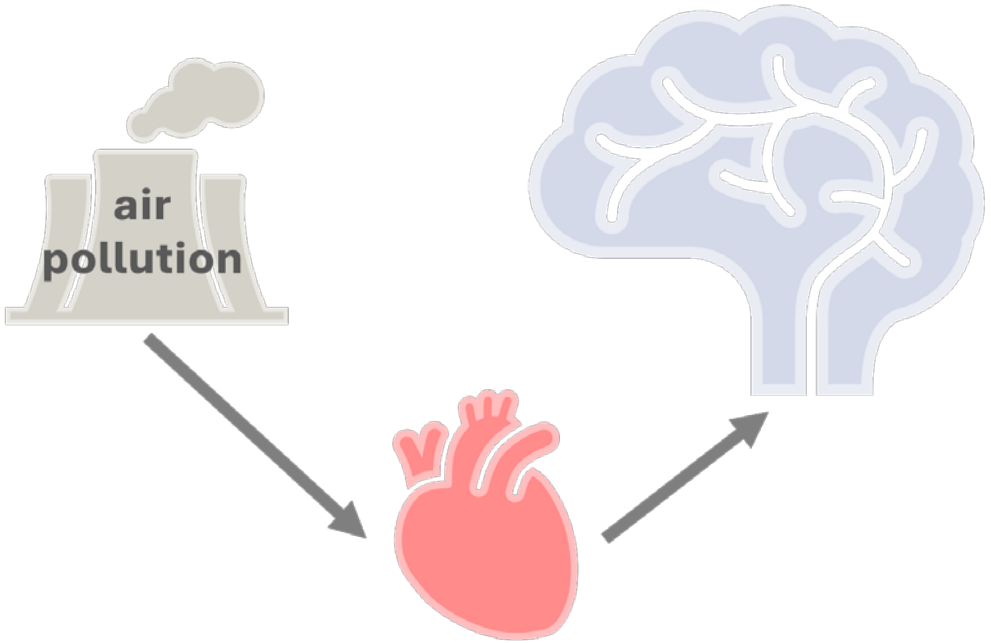


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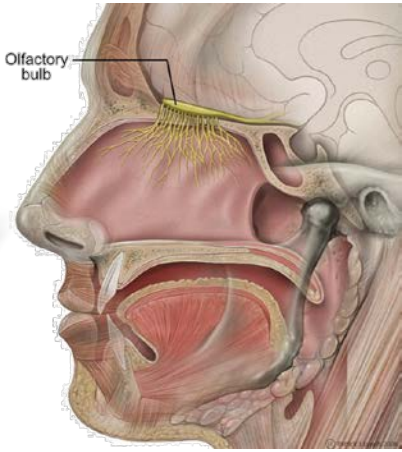
**Air pollution might access the brain**
via lungs or intranasal pathway

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# State of the epidemiologic science on air pollution and dementia

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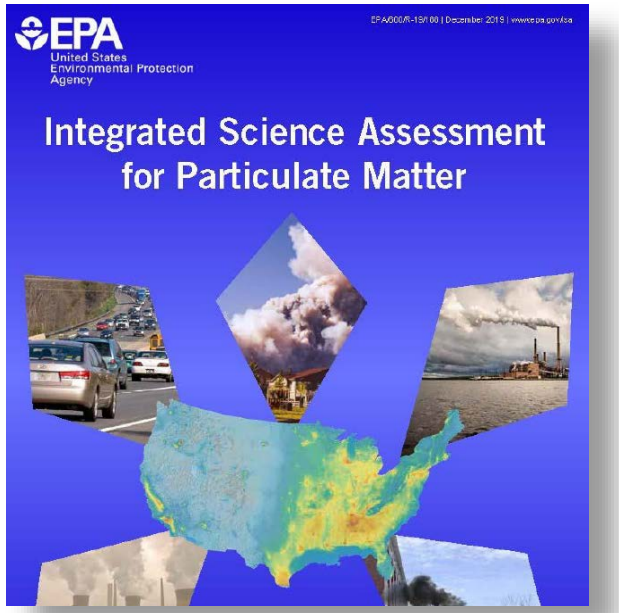
# Sources

Systematic review:
Weuve et al. EHP (2021)


Systematic review: Wilker et al. BMJ (2023)


US EPA Integrated Science Assessment for Particulate Matter (2019)

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RECOGNITION BY **ADVISORY INITIATIVES**

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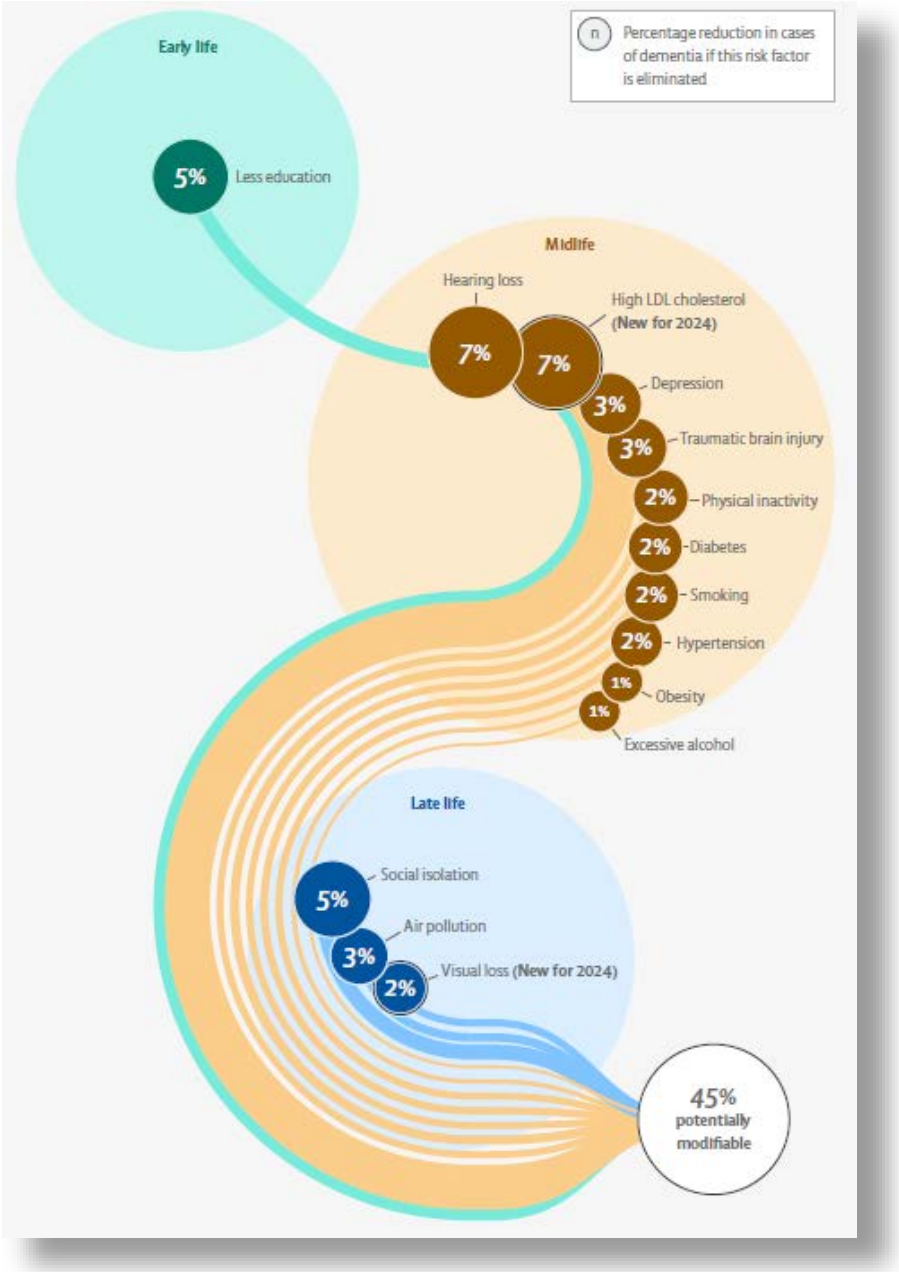


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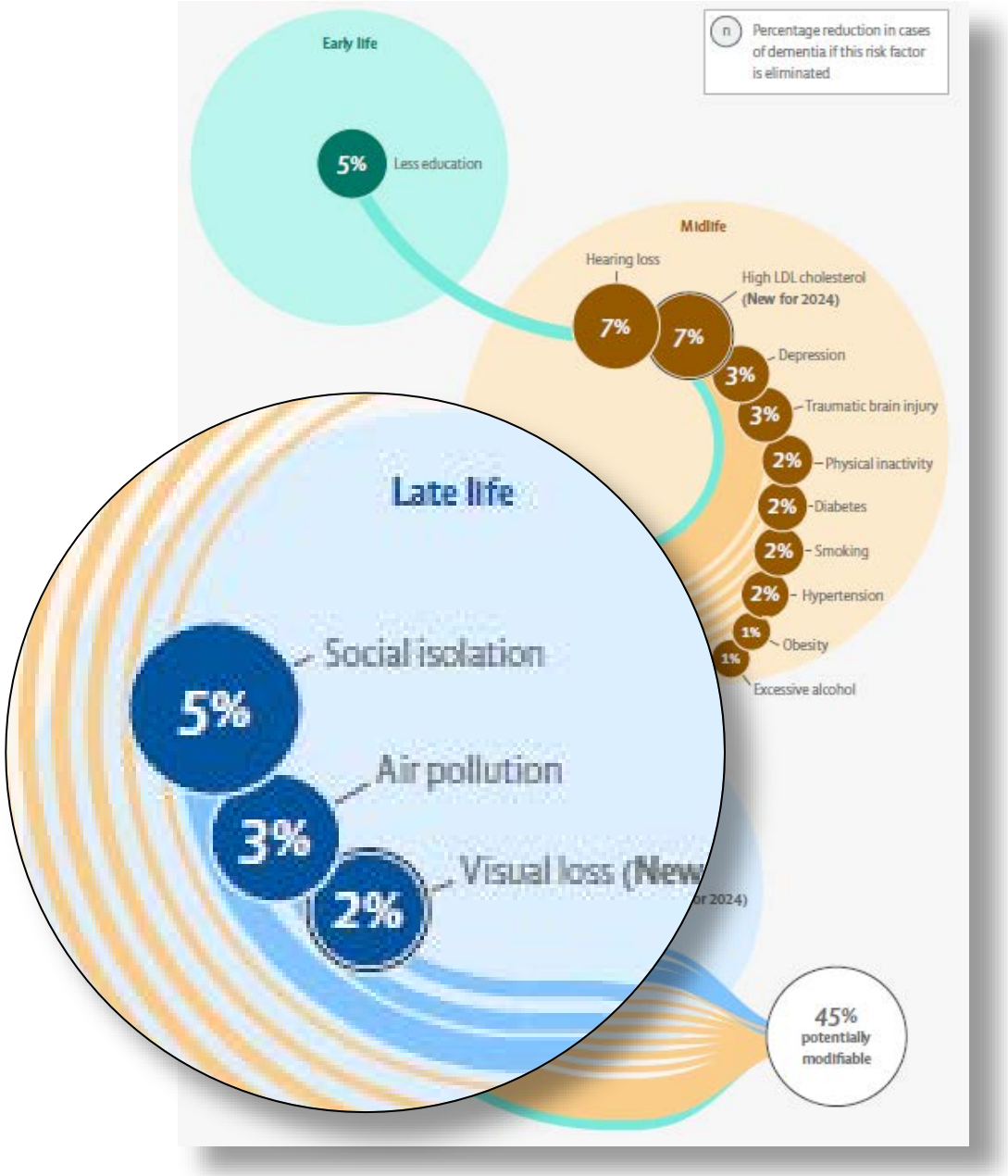


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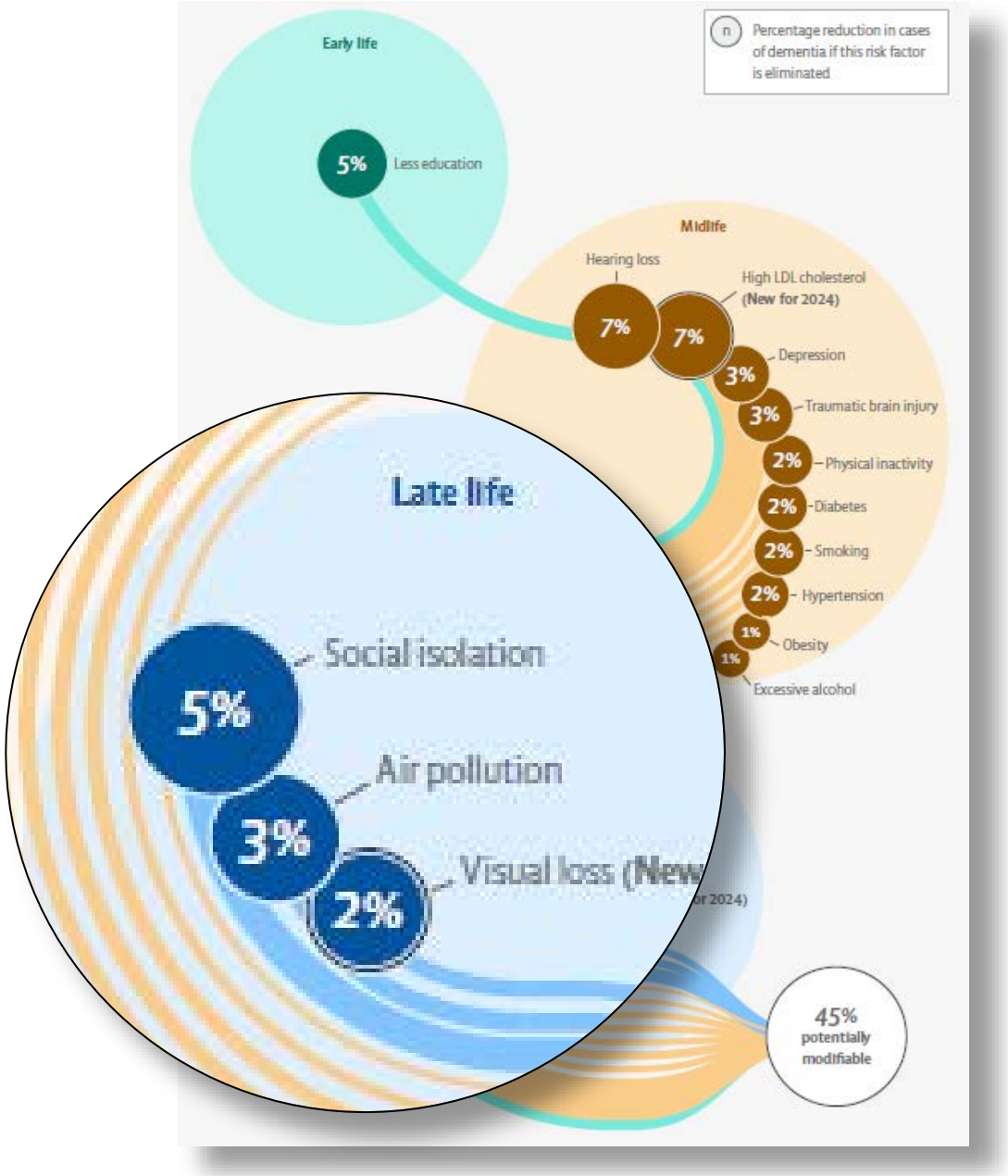


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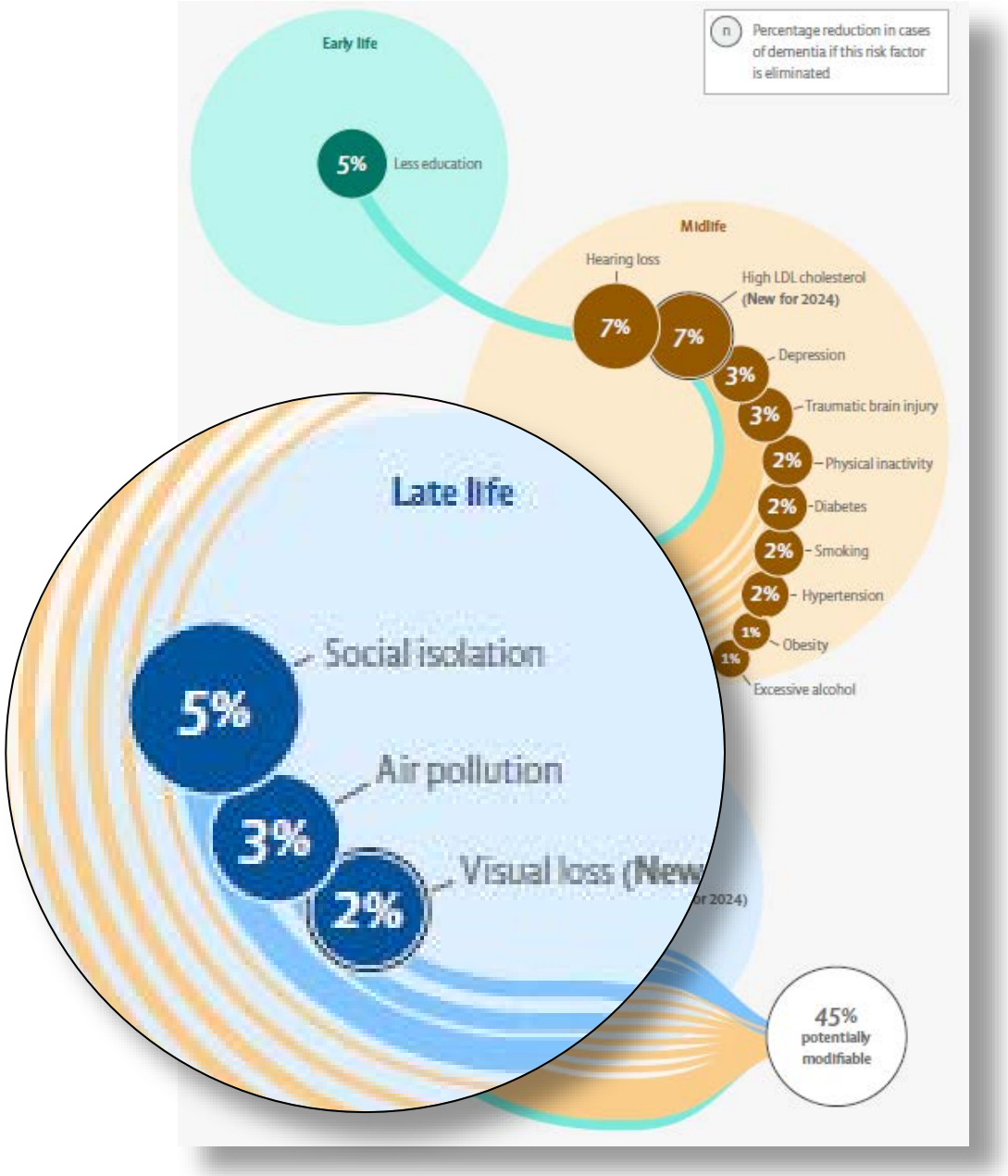


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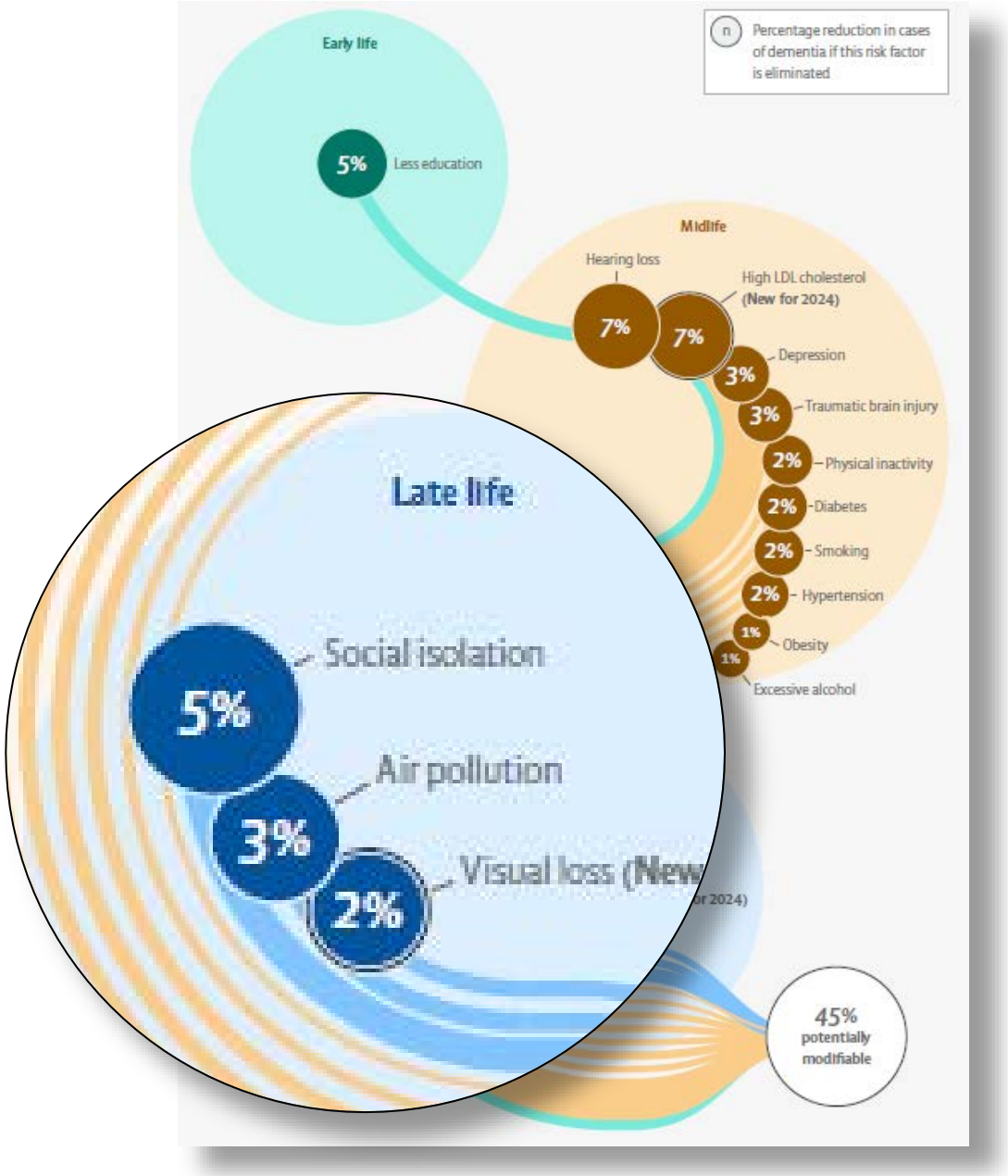
- Feb 2024: **US EPA tightened regulatory standard** for annual $PM_{2.5}$ concentration:
  - from 12 to 9 μg/m³

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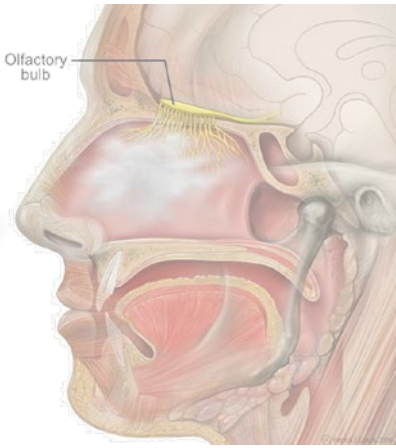


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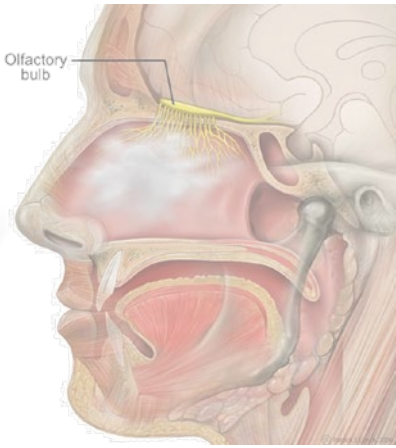


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We characterized nanoparticles in olfactory bulbs of deceased participants of Rush's Religious Orders Study …

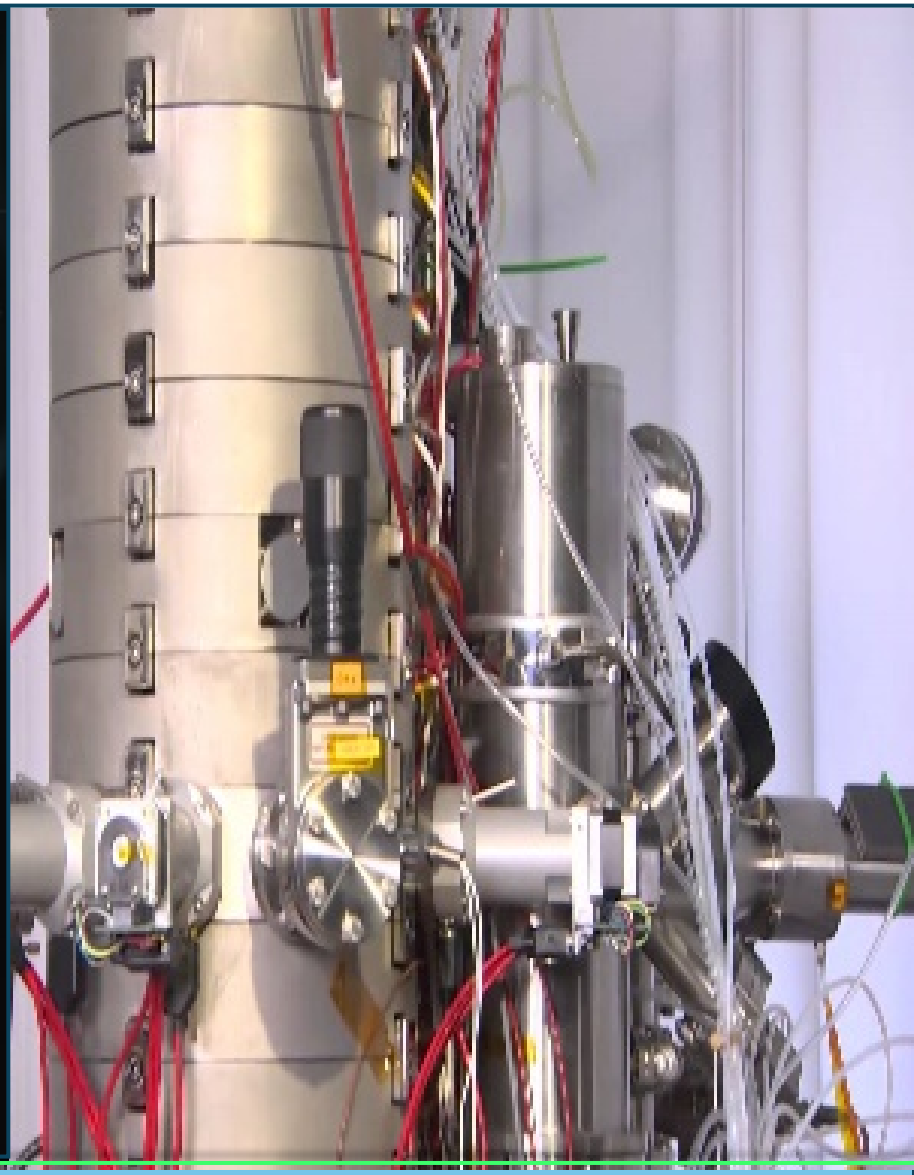
(Uschi Graham et al. In preparation. R01AG067497)

(Graham et al. Chemical Research in Toxicology 2020 PMC7774012.)

**Analytical imaging** via high-resolution scanning transmission electron microscopy (**STEM**)

... coupled with **chemical analysis** via

- electron energy loss spectroscopy (**EELS**)
- energy dispersive X-ray spectroscopy (**EDX**)



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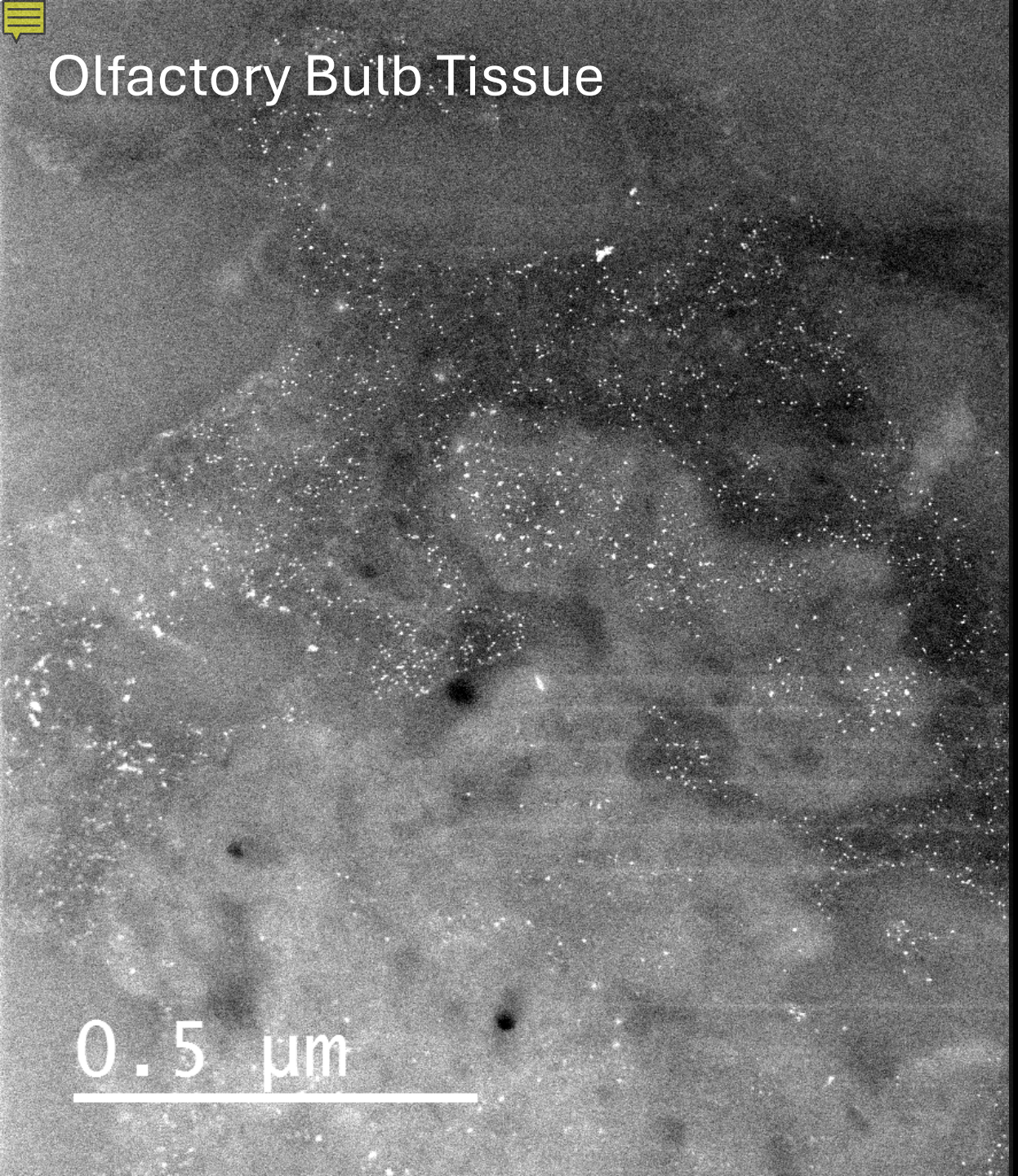
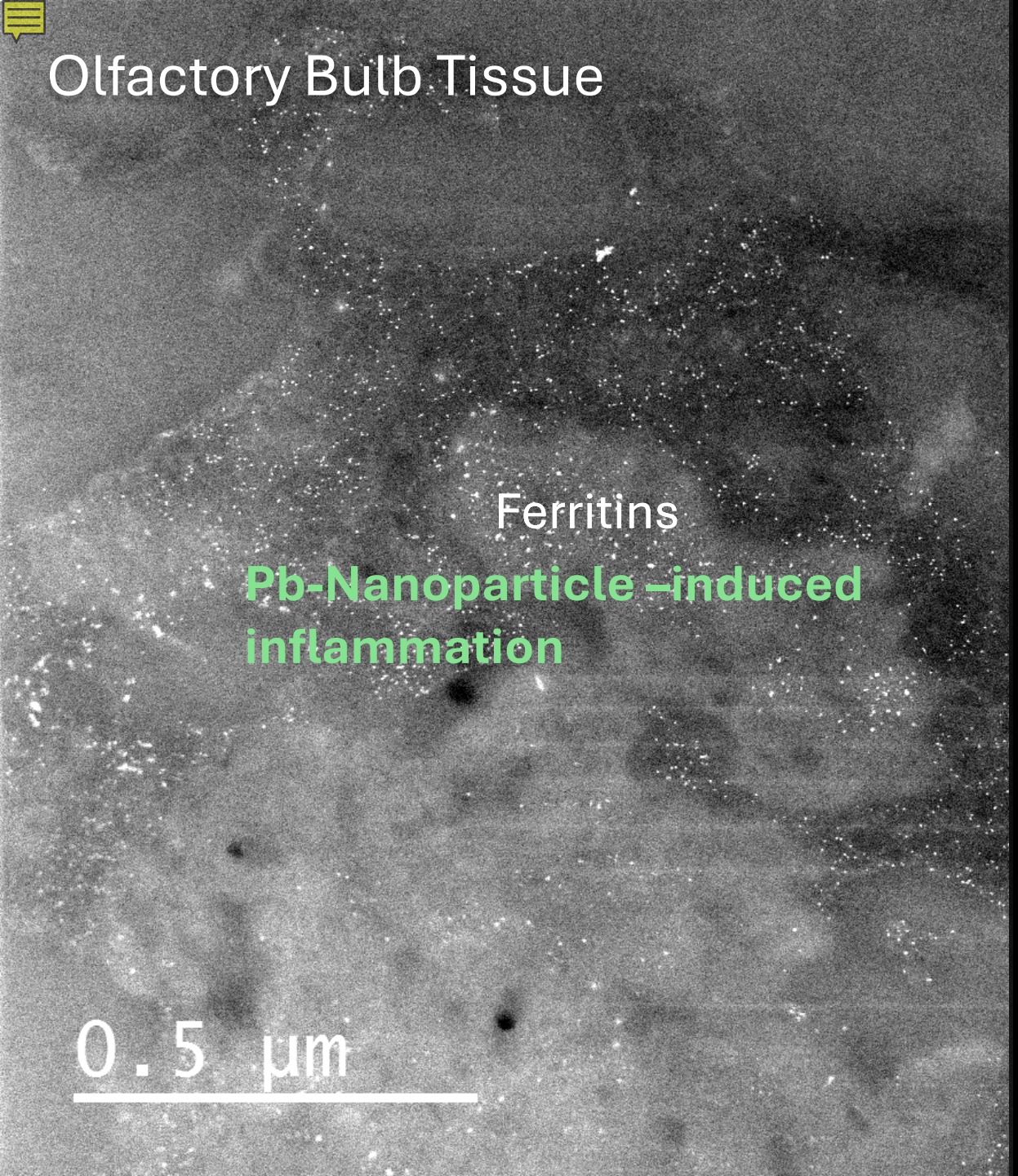

Olfactory Bulb Tissue
0.5 µm


Olfactory Bulb Tissue
Ferritins
Pb-Nanoparticle –induced inflammation
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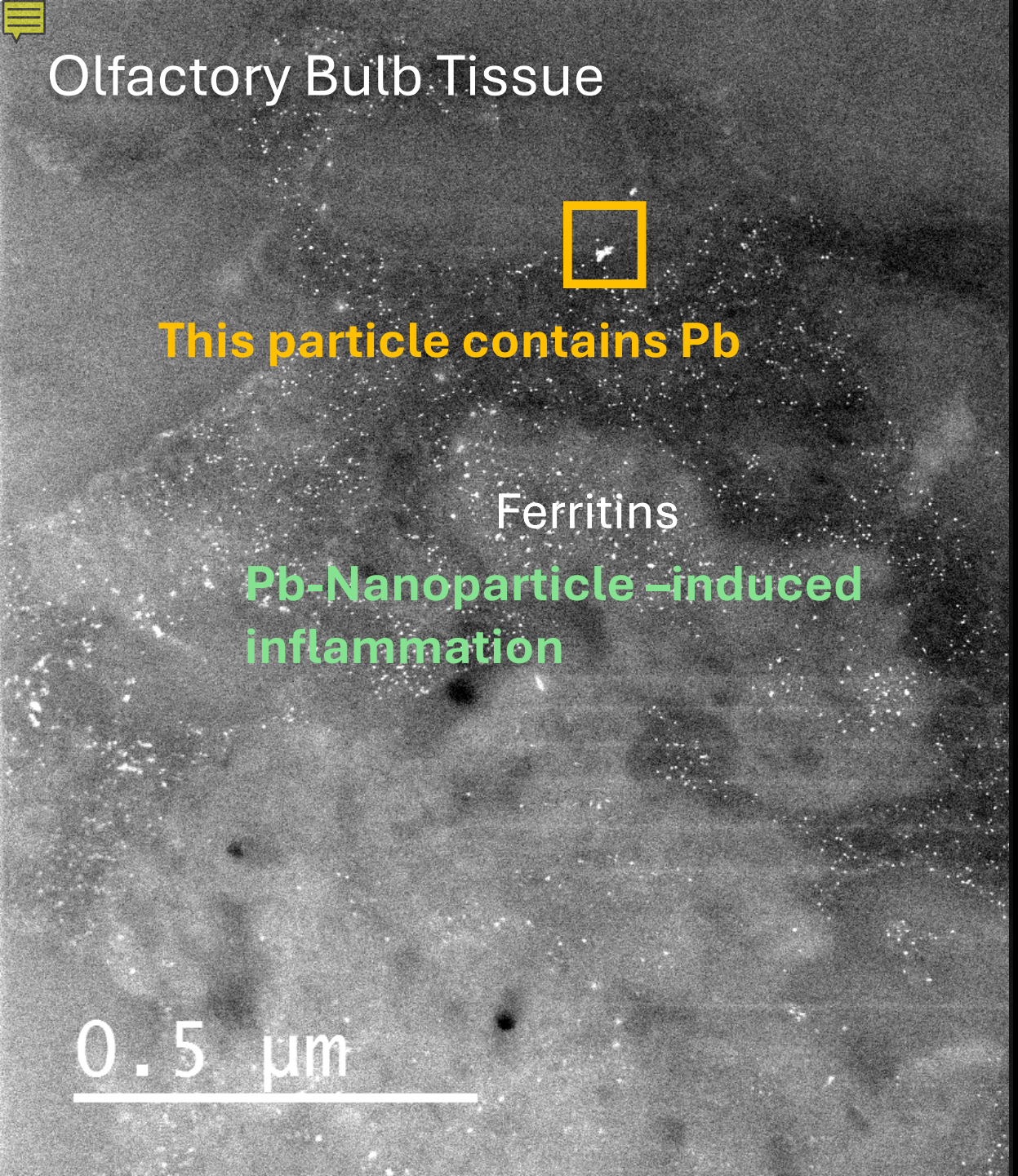
Olfactory Bulb Tissue
This particle contains Pb
Ferritins
Pb-Nanoparticle –induced inflammation
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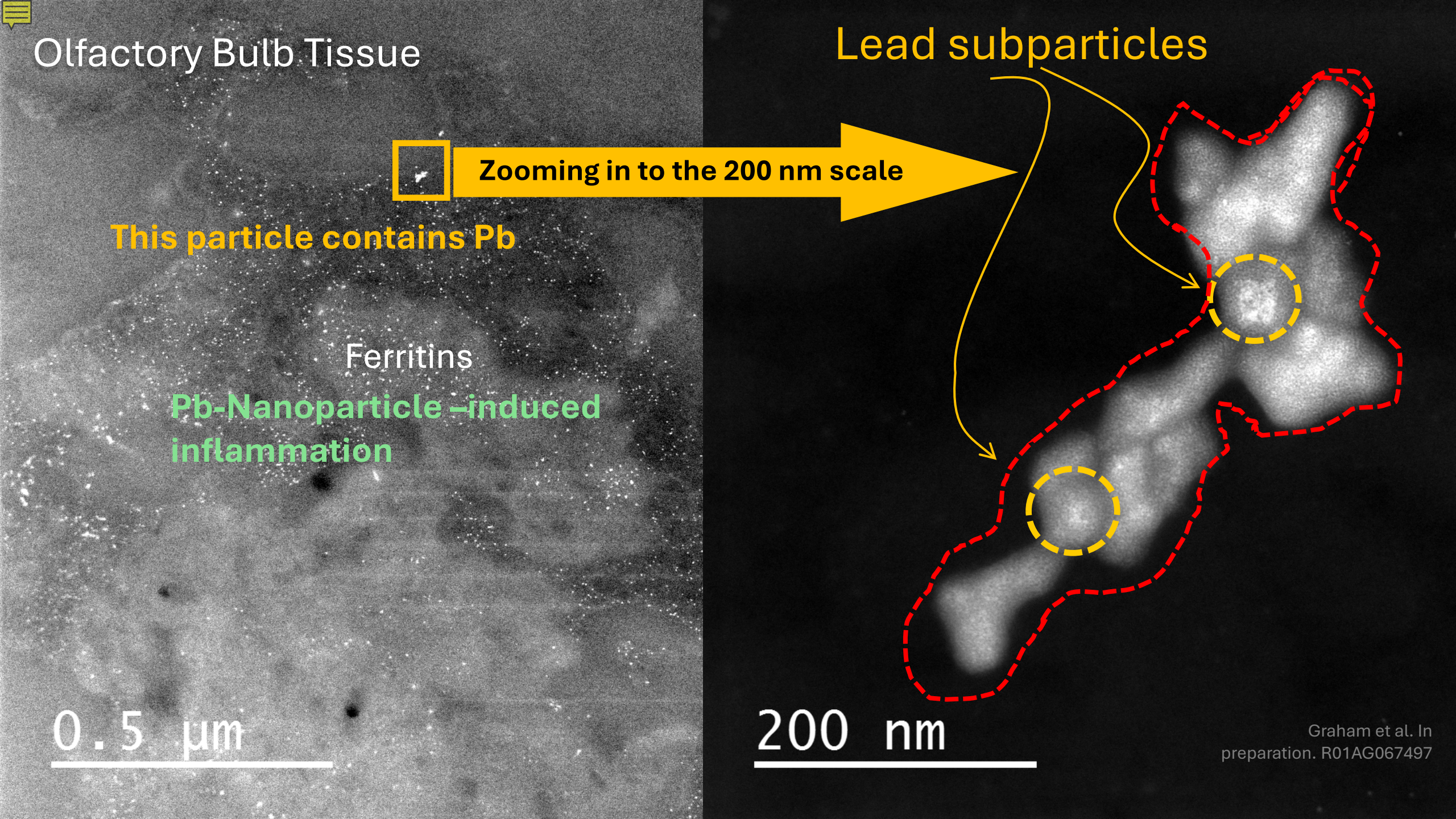
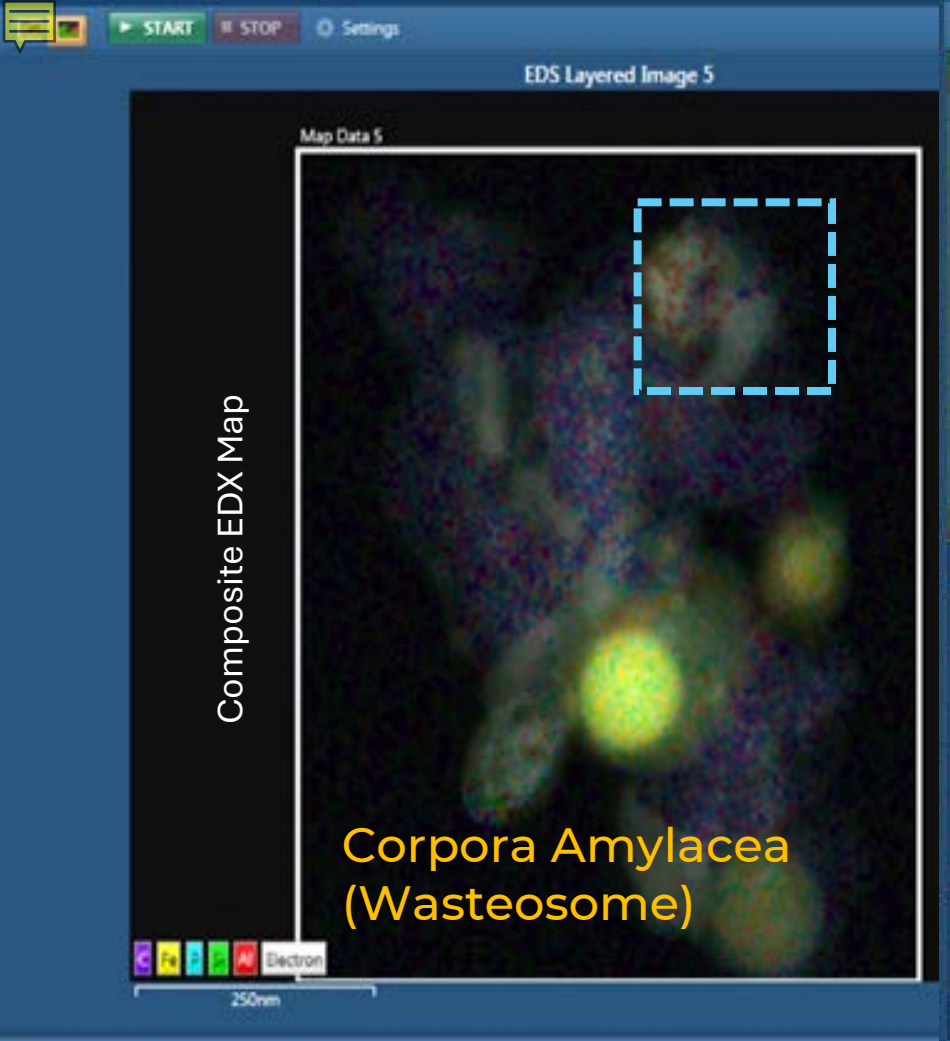
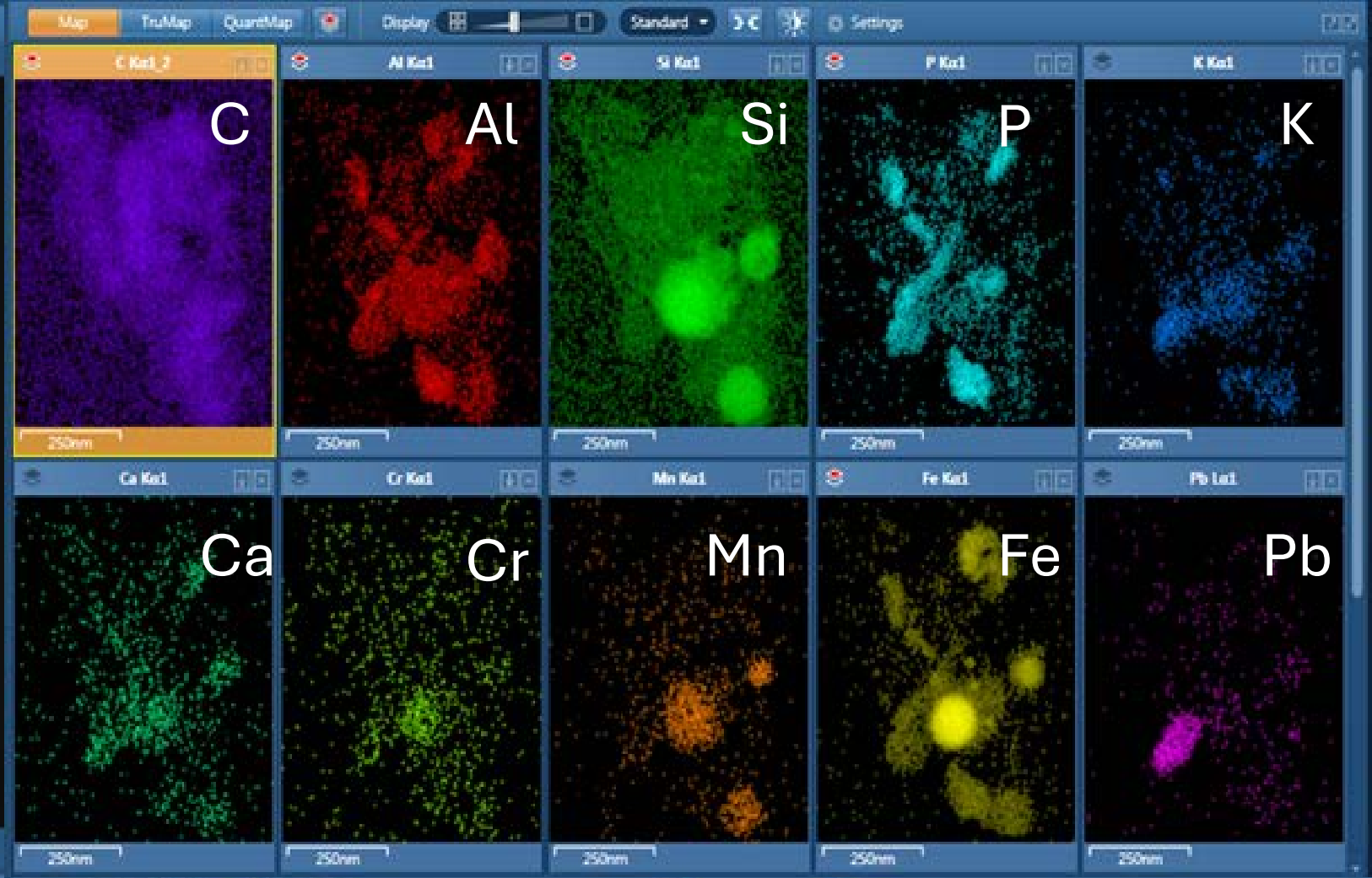
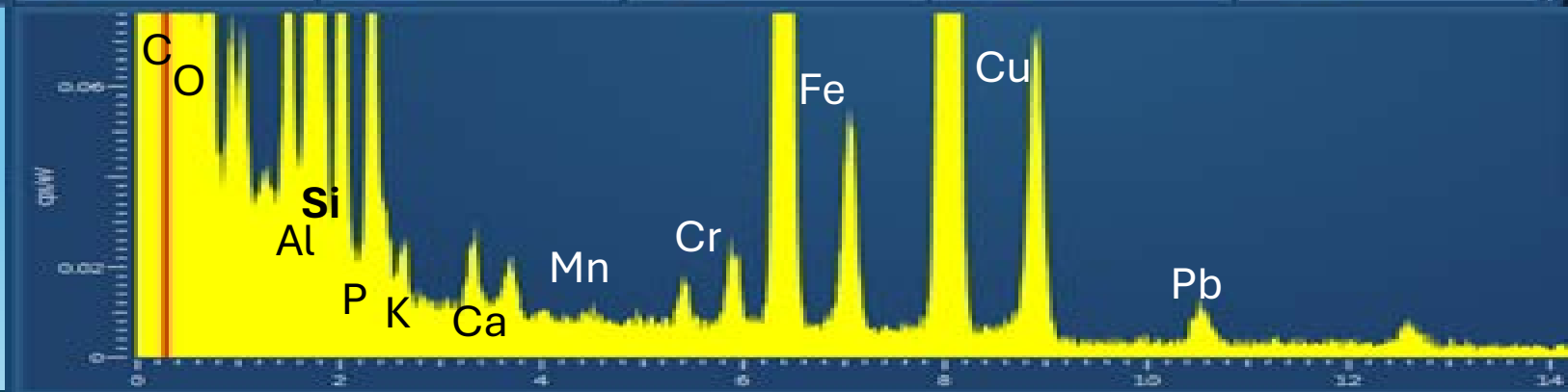

Olfactory Bulb Tissue
Zooming in to the 200 nm scale
This particle contains Pb
Ferritins
Pb-Nanoparticle –induced inflammation
0.5 µm
Lead subparticles
200 nm
Graham et al. In preparation. R01AG067497




# Nanoparticles inside Olfactory Bulb

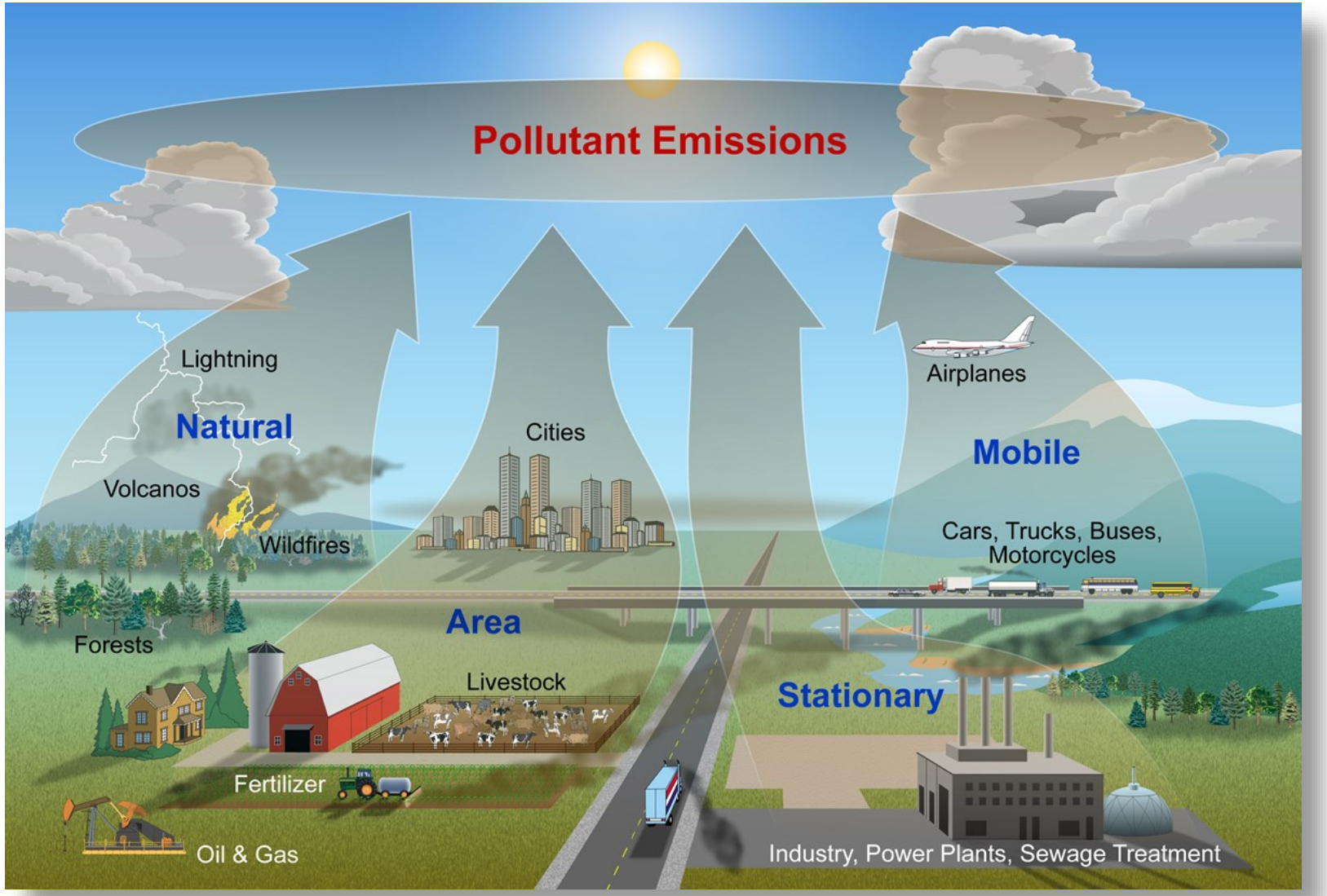



Graham et al. In preparation. R01AG067497

# Recent development 3:
# Examination of air pollution sources

Examples:

- Road traffic
- Coal-burning
- Agriculture
- Aviation
- Wildfire

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# Systematic review of the health effects of traffic-related air pollution: HEI (2022)

## SCOPE

| Mostly $NO_2$ and $NO_x$ | Cognition<br>Cognitive decline<br>Dementia | 9 studies<br><br>(adults, mostly 65+) |
|---|---|---|
| Some $PM_{10}$, $PM_{10-2.5}$, $PM_{2.5}$, BC, traffic proximity | | |

HEI Panel on the Health Effects of Long-Term Exposure to Traffic-Related Air Pollution. 2022.

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Cognition
Cognitive decline
Dementia

9 studies

(adults, mostly 65+)

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## CONCLUSIONS

"**low to moderate confidence**" that evidence is consistent with adverse association

Mostly based on assns of **$NO_2$** and **$NO_x$** with **cognition**

Weak support with respect to cognitive decline

# Recent development 3:
# … air pollution sources: road traffic

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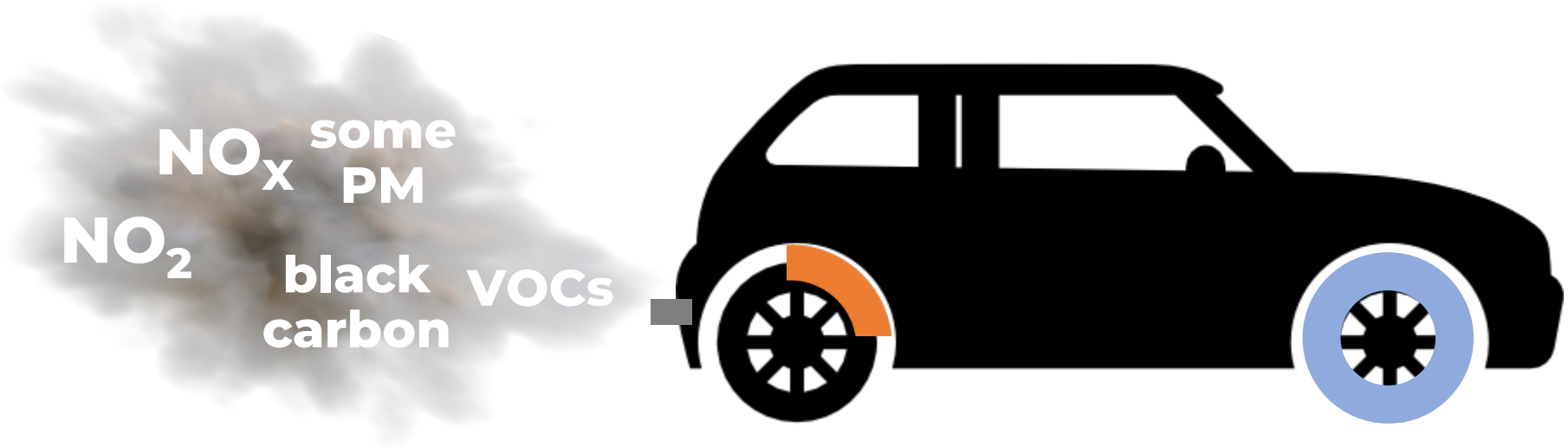
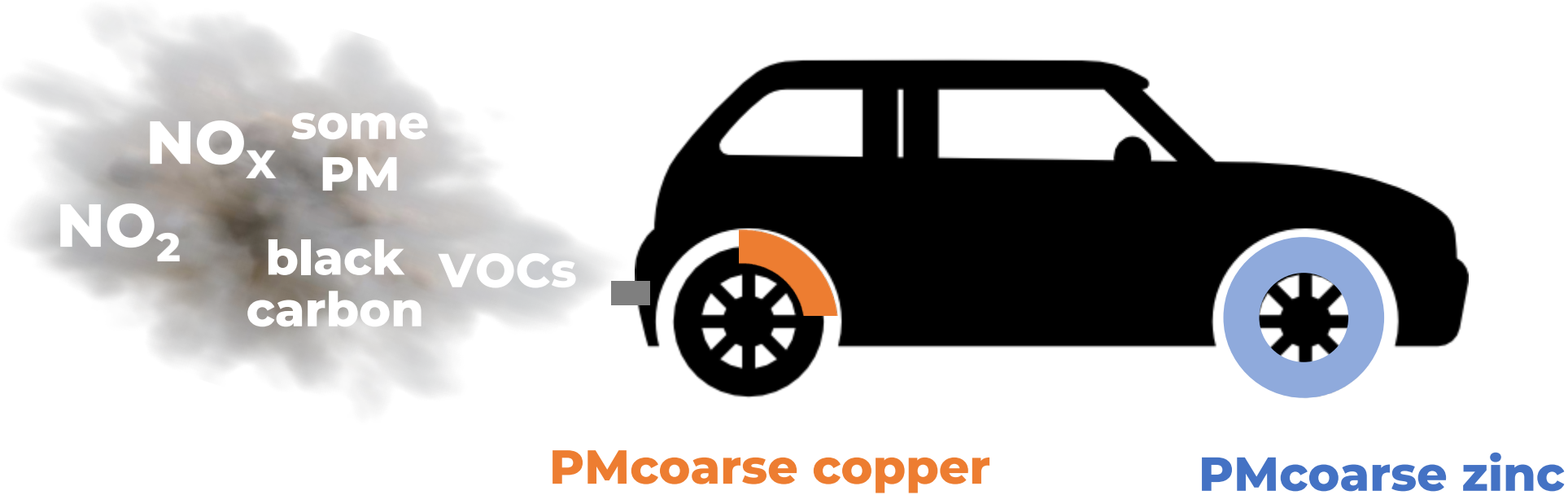
# Recent development 3:
# … air pollution sources: road traffic




Jennifer Weuve, ScD jweuve@bu.edu

# Recent development 3:
# … air pollution sources: road traffic




Jennifer Weuve, ScD jweuve@bu.edu

# Recent development 2:
# … air pollution sources: road traffic

Association of **long-term exposure to traffic-related air pollution** with **rate of cognitive decline**

- Chicago Health and Aging Project

Credit: Stephanie Grady

(Andrews et al. EHP 2024; PMC11623384; R01AG065359)

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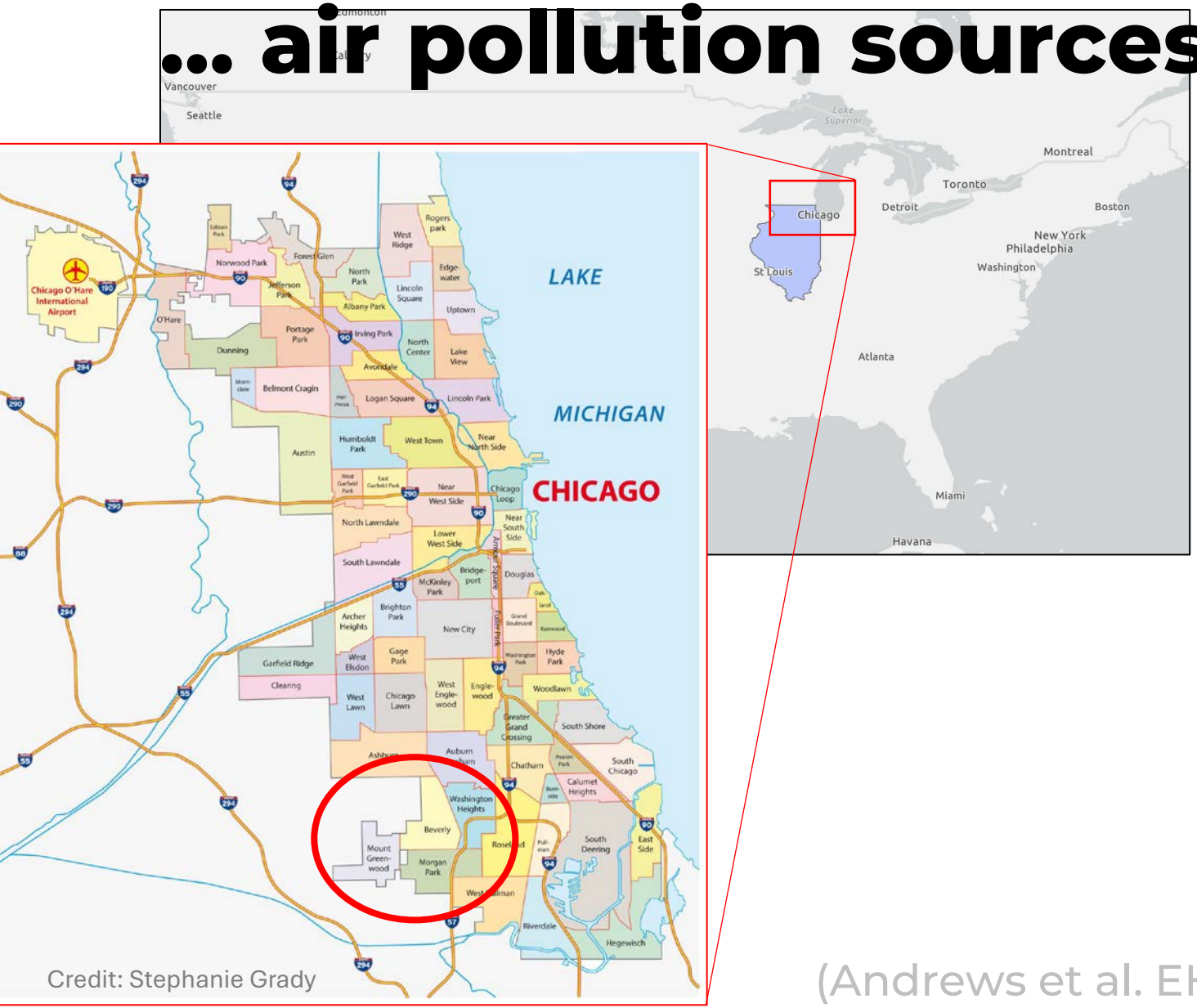
# … air pollution sources: road traffic




Credit: Stephanie Grady

Association of **long-term exposure to traffic-related air pollution** with **rate of cognitive decline**

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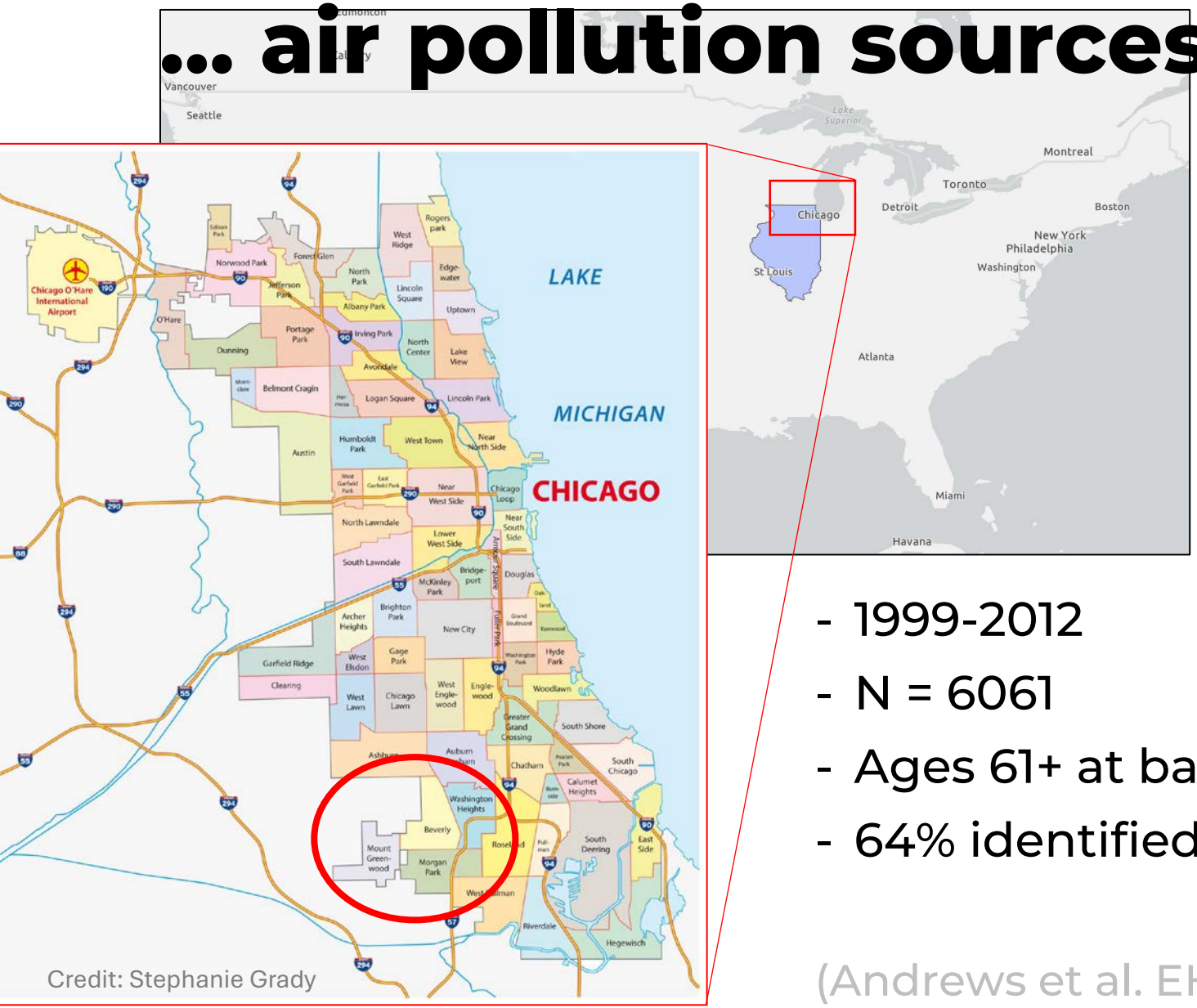


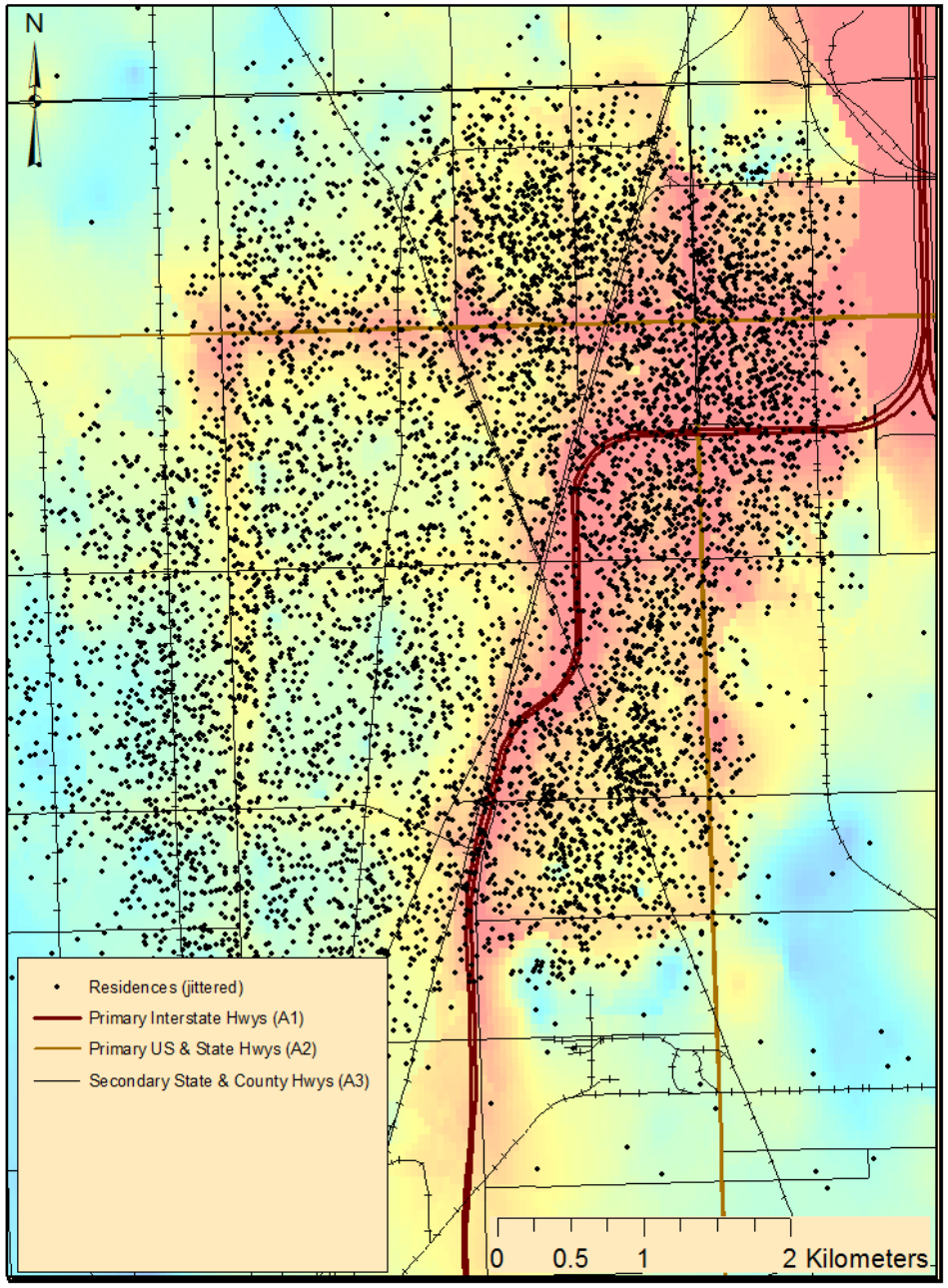

Credit: Stephanie Grady

Association of **long-term exposure to traffic-related air pollution** with **rate of cognitive decline**

- Chicago Health and Aging Project

- 1999-2012
- N = 6061
- Ages 61+ at baseline
- 64% identified as Black, 36% as White

(Andrews et al. EHP 2024; PMC11623384; R01AG065359)




$NO_x$ (ppb)

45

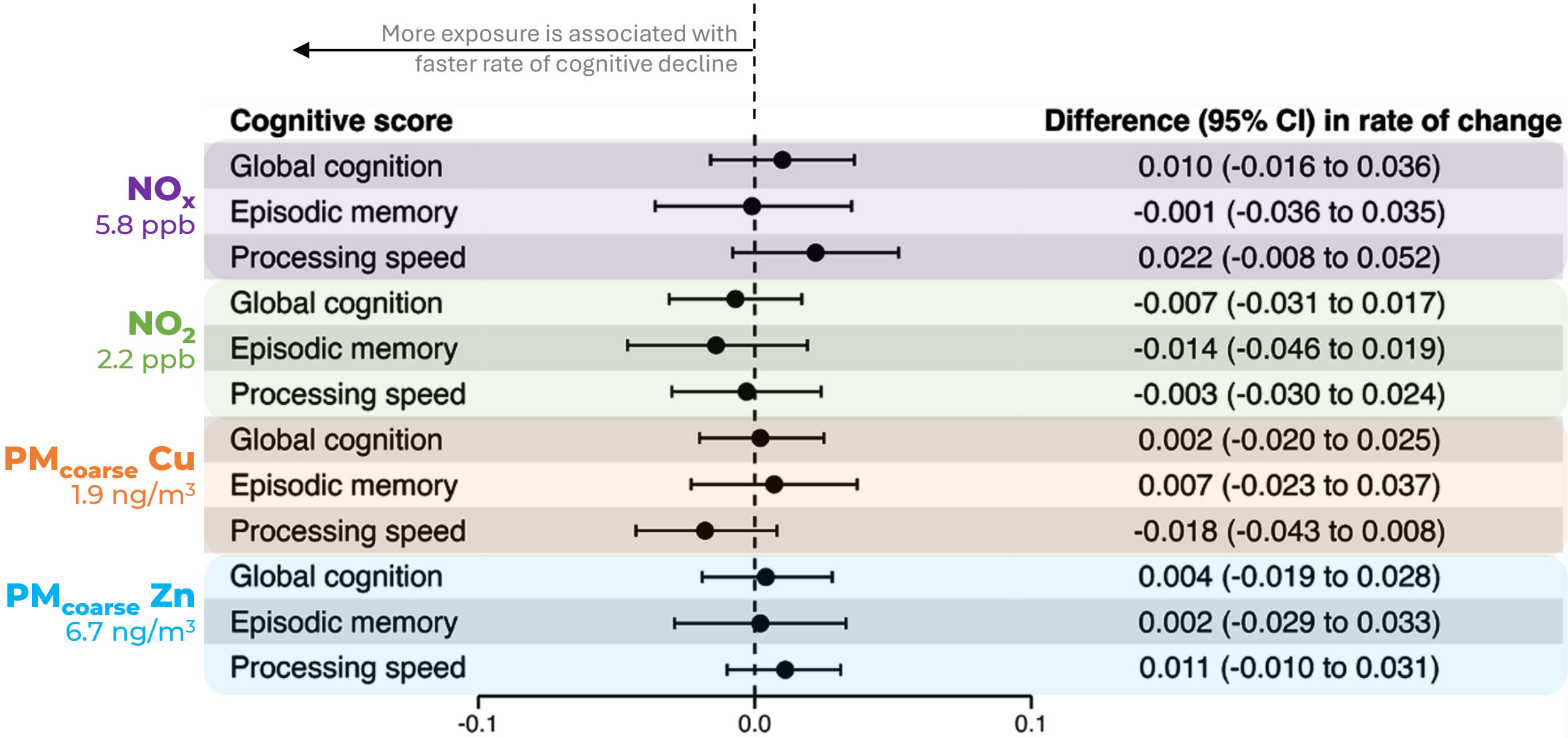
35

25

15

Mean predicted annual $NO_x$ concentration, ppb, (1999-2011) in the CHAP area

Weuve et al.
*EHP*, 2016




Adjusted difference in mean 5-year change in cognitive score per SD-increment in 3-y pollutant exposure

(Andrews et al. EHP 2024; PMC11623384; R01AG065359)

# Long-term exposure to $PM_{2.5}$, by source, in relation to incident dementia

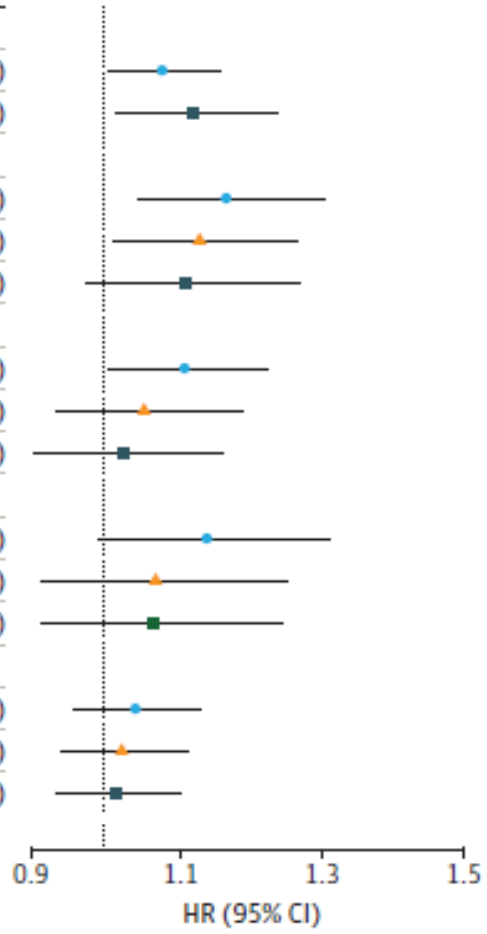
- Health and Retirement Study
- N = 27,857
- 1998-2016

Zhang et al. JAMA Int Med 2023

Jennifer Weuve, ScD jweuve@bu.edu

**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) | |
| Model 1 | 1.05 (0.96-1.14) |
| Model 2 | 1.03 (0.94-1.12) |
| Model 3 | 1.02 (0.93-1.11) |




| 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) |
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| Model 3 | 1.05 (1.02-1.08) |
| Windblown dust (0.0-0.1) | |
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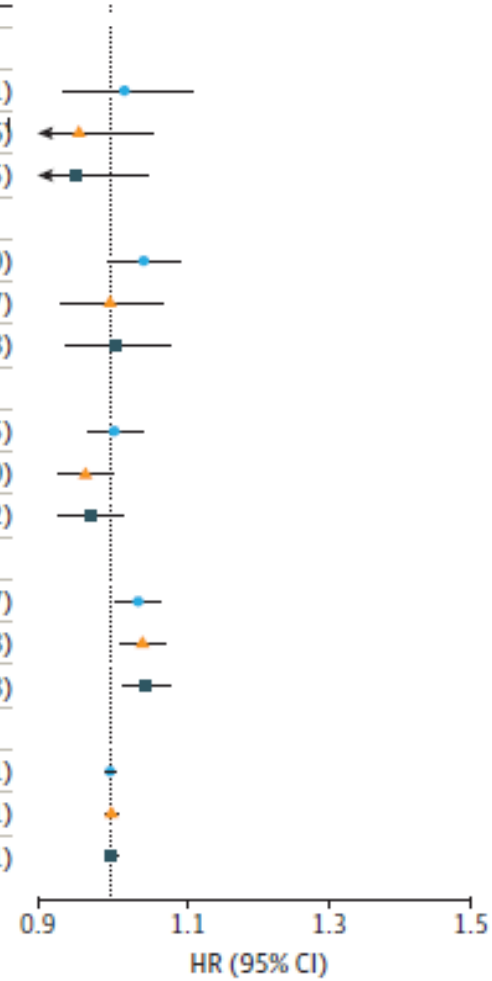
| Model 2 | 1.00 (1.00-1.01) |
| Model 3 | 1.00 (0.99-1.01) |




Zhang et al. JAMA Int Med 2023

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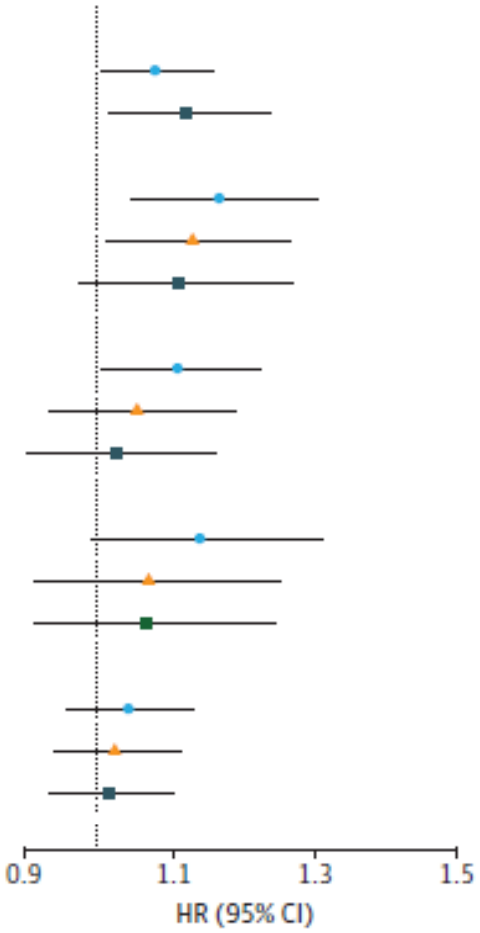


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| Model 1 | 1.05 (1.00-1.10) |
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| Industry other (0.7-1.2) | |
| Model 1 | 1.01 (0.97-1.05) |
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| Model 1 | 1.04 (1.01-1.07) |
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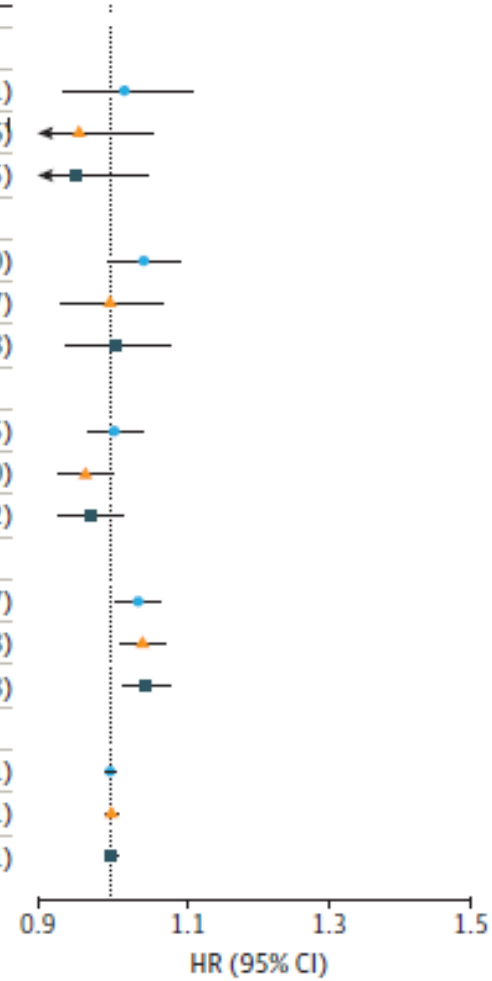


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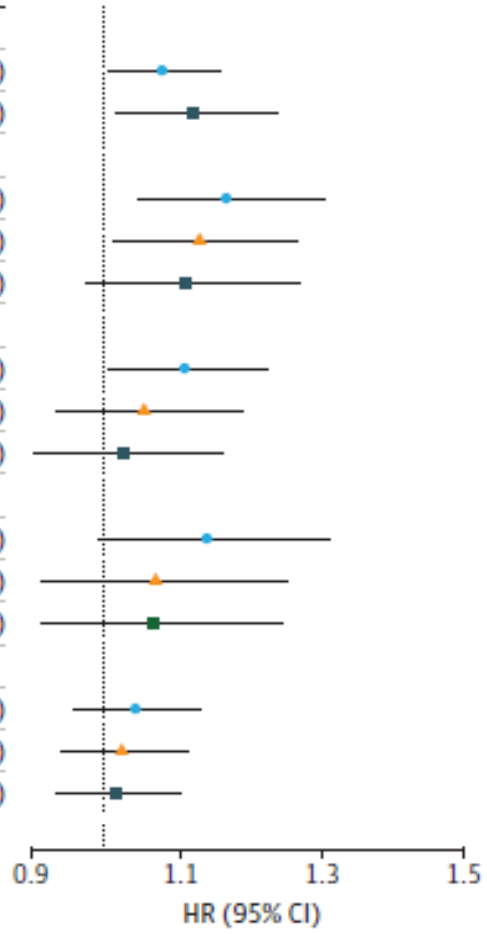


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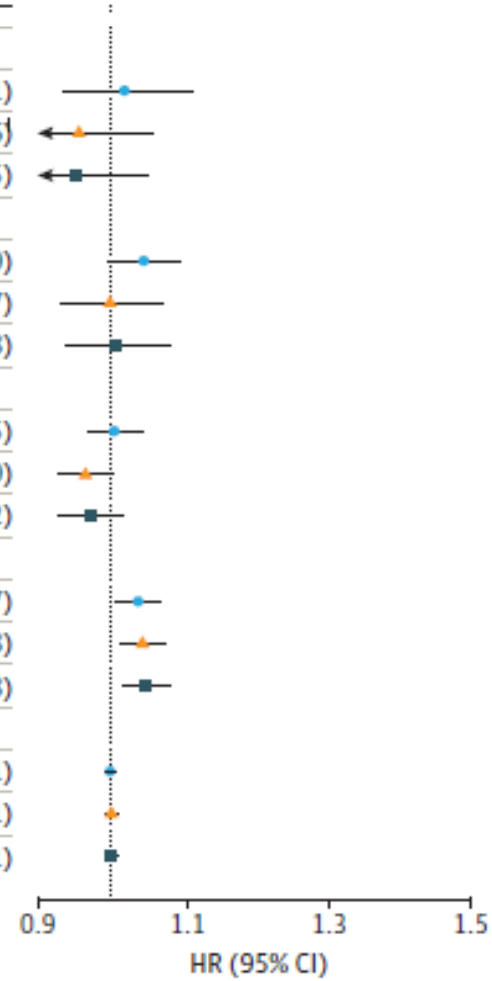


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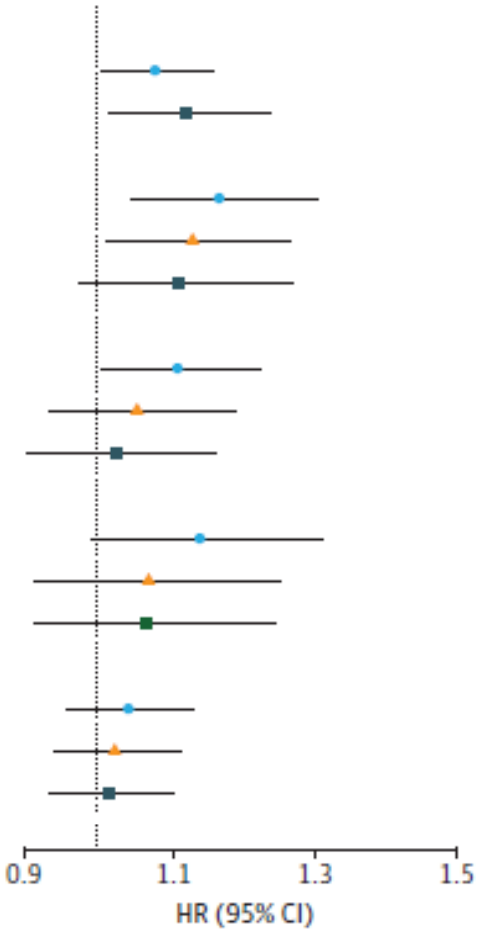


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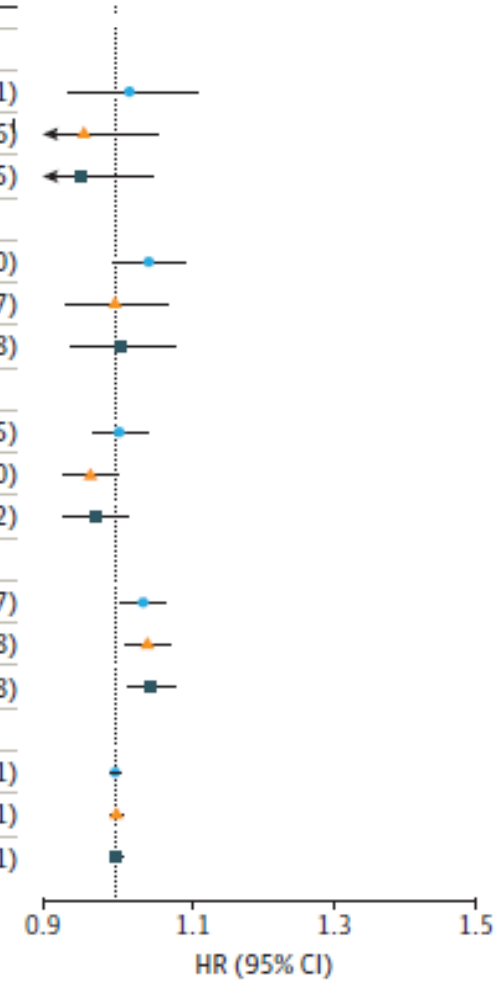


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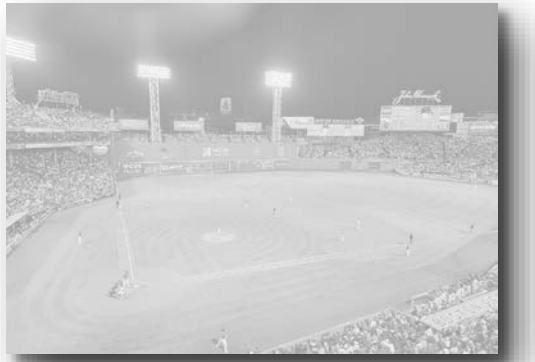
NOISE:
unwanted and/or
harmful sound

# Environmental (community) noise emanates from outside our homes and places of work and learning

Kevin Read


Grady et al. In preparation.
R01AG065359

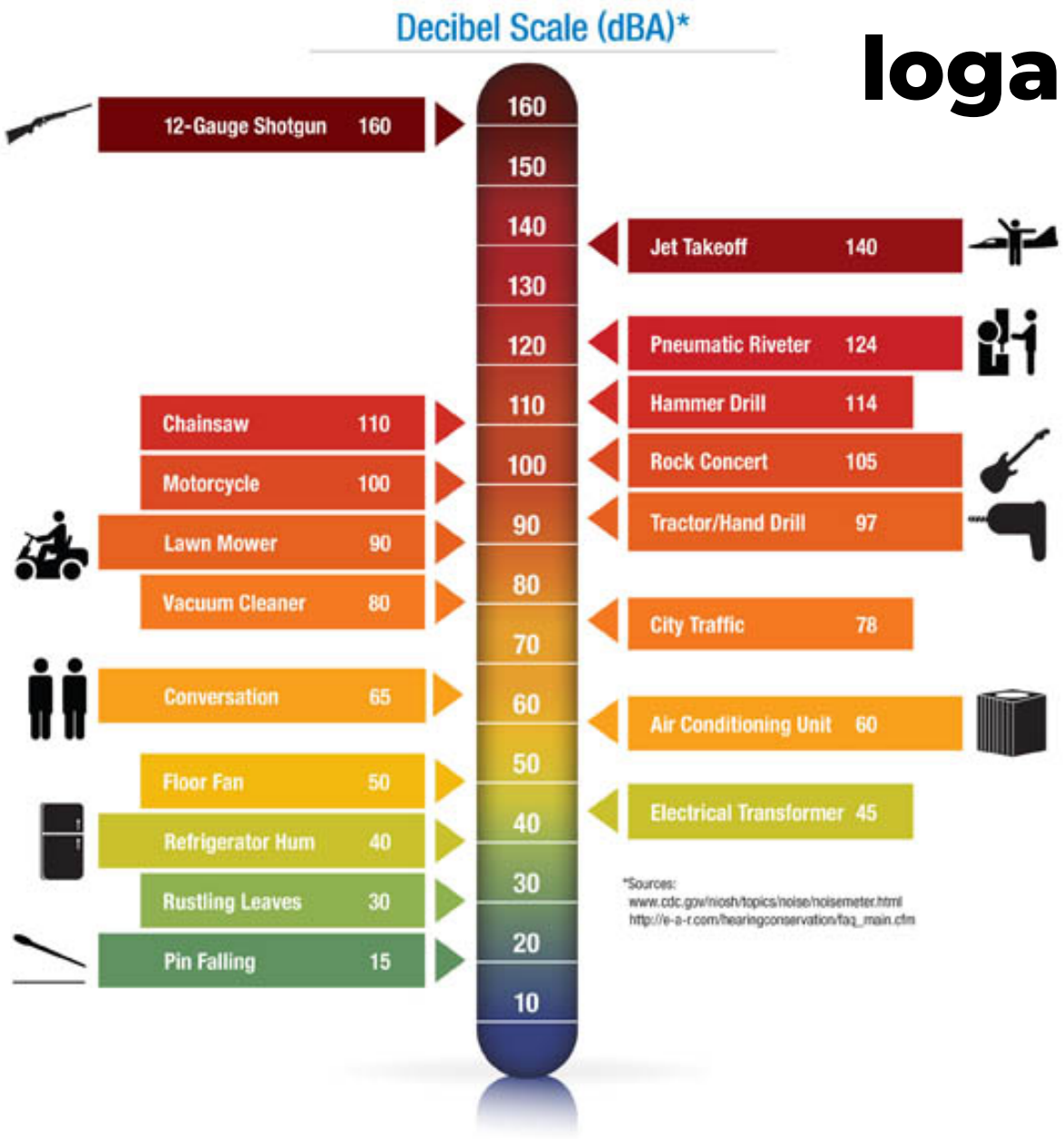
# Environmental (community) noise emanates from outside our homes and places of work and learning



Kevin Read


Grady et al. In preparation.
R01AG065359

# Noise is measured logarithmically in decibels




| Decibel Change | Perceived Loudness | Relative Intensity |
|---|---|---|
| +10 | x2 | x10 |
| +20 | x4 | x100 |
| +30 | x8 | x1,000 |

Grady et al. In preparation.

R01AG065359

# How might noise influence the development of dementia?


Grady et al. In preparation. R01AG065359. Modified from Münzel et al. 2017 and Babisch et al. 2013

# How might noise influence the development of dementia?


Sleep

Stress

Stress response

Grady et al. In preparation. R01AG065359. Modified from Münzel et al. 2017 and Babisch et al. 2013

# How might noise influence the development of dementia?


Sleep

Stress

ANS

Endocrine system

Grady et al. In preparation. R01AG065359. Modified from Münzel et al. 2017 and Babisch et al. 2013

Stress response

Biological activation

# How might noise influence the development of dementia?


Sleep

Stress

ANS

Endocrine system

Blood glucose

Inflammation

Oxidative stress

Endothelial dysfunction

Blood pressure

Stress response

Biological activation

Increased chronic stress-related factors

Grady et al. In preparation. R01AG065359. Modified from Münzel et al. 2017 and Babisch et al. 2013

# How might noise influence the development of dementia?

Noise source

Sleep

Stress

ANS

Endocrine system

Blood glucose

Inflammation

Oxidative stress

Endothelial dysfunction

Blood pressure

CVD

Dementia

Stress response

Biological activation

Increased chronic stress-related factors

Disease

Grady et al. In preparation. R01AG065359. Modified from Münzel et al. 2017 and Babisch et al. 2013

# Long-term exposure to noise in relation to cognition, rate of cognitive decline, and dementia incidence

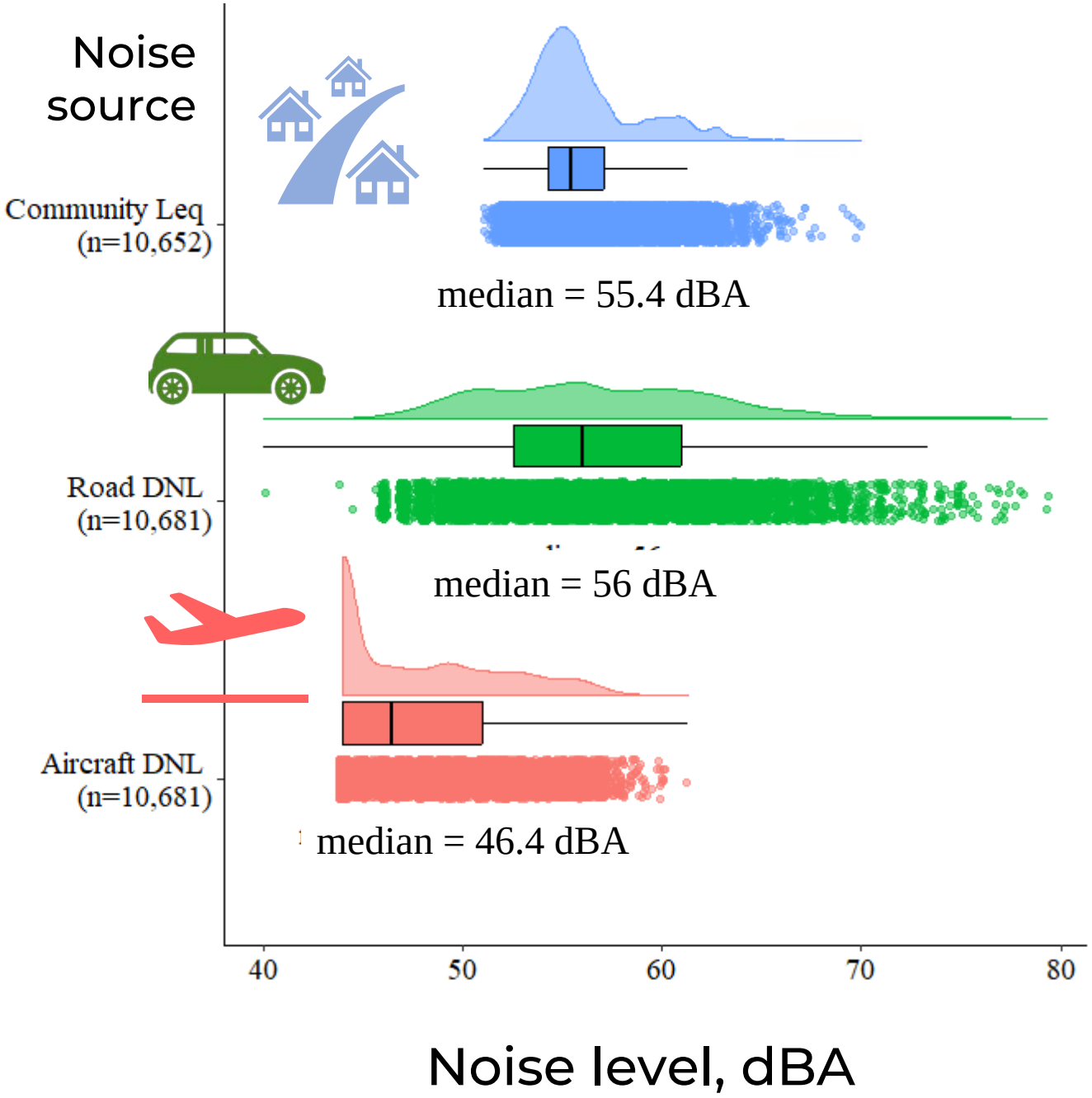
In the Chicago Health and Aging Project

- 1993-2012
- N = 10,232
- Ages 61+ at baseline
- 64% identified as Black, 36% as White

(Stephanie Grady et al. In preparation. R01AG065359)

Jennifer Weuve, ScD jweuve@bu.edu

# Distribution of noise levels outside CHAP residences



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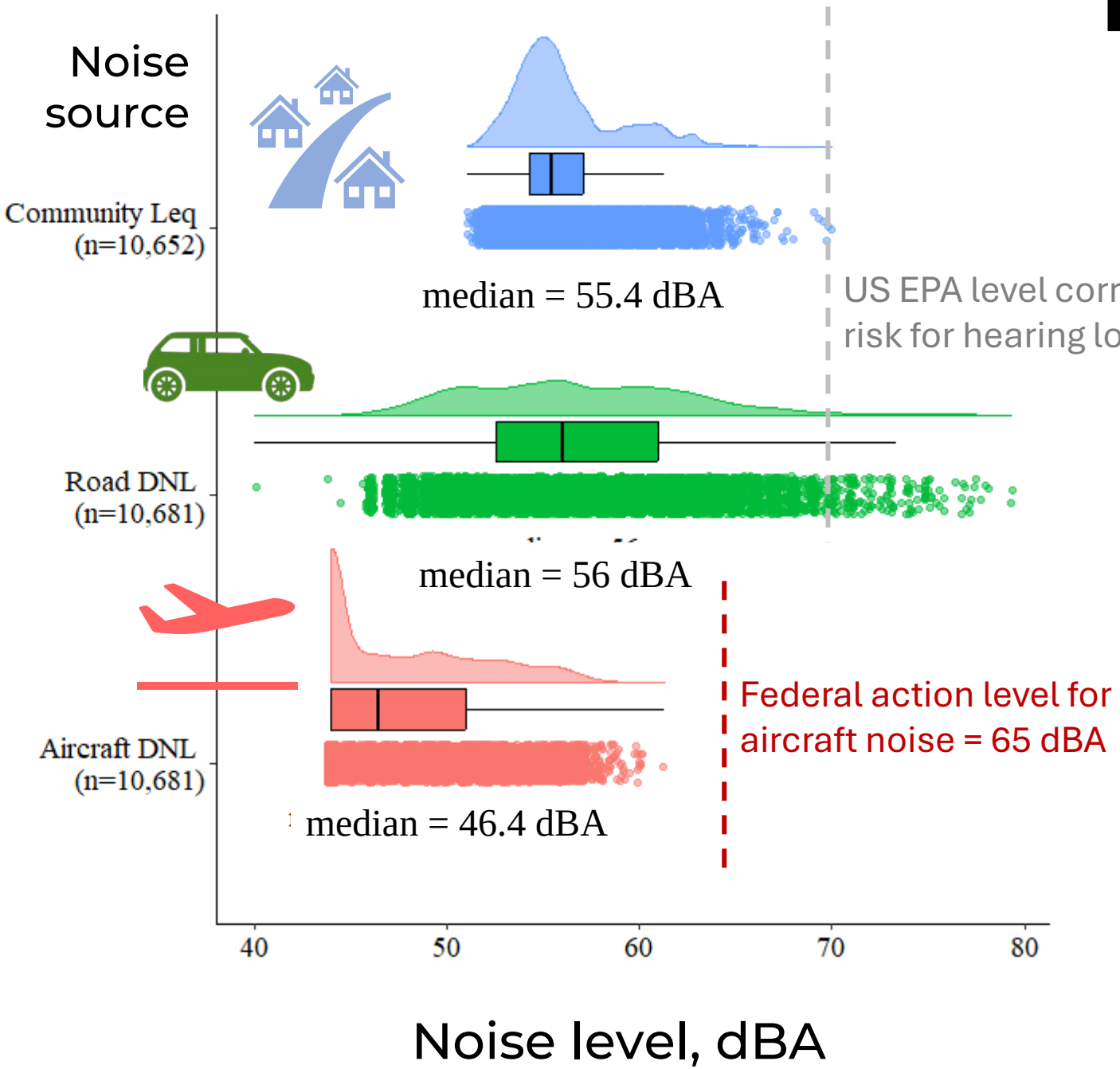
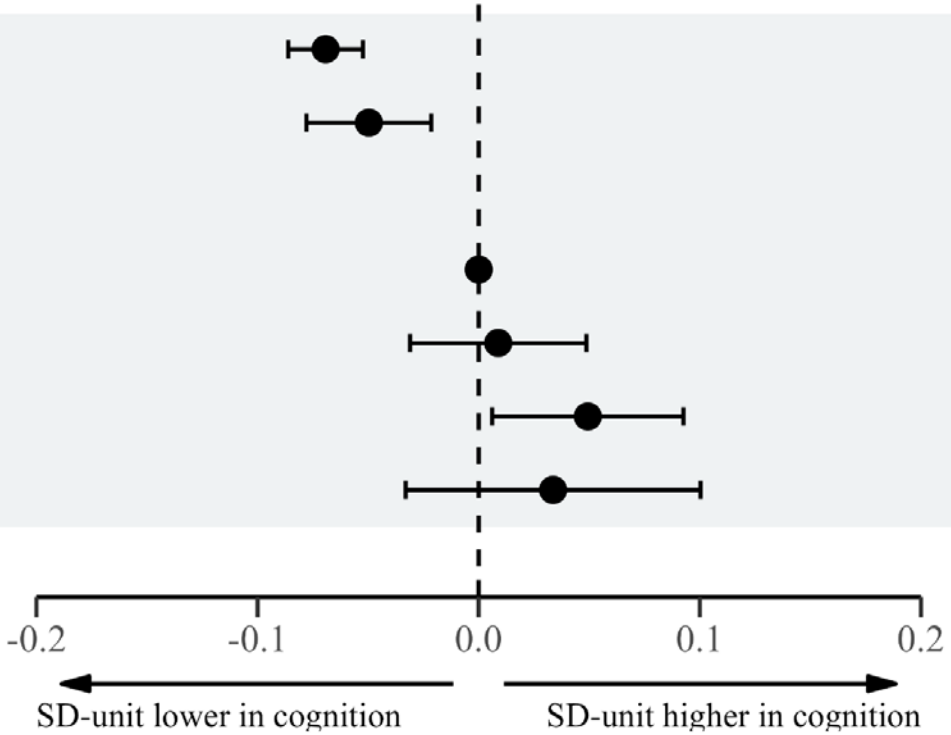


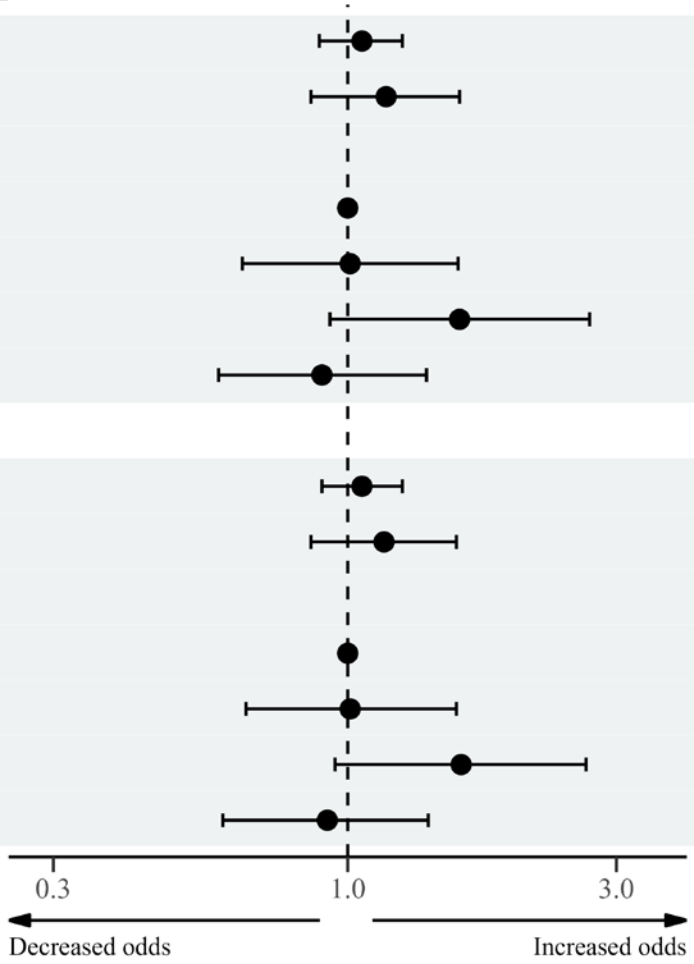
# Association of noise with cognitive performance

| Noise measure | N obs / N participants | Difference in baseline level, SD-units (95% CI) |
|---|---|---|
| Community Leq (per 2.8 dBA) | 27,003 / 10,204 | -0.069 (-0.086, -0.052) |
| Road DNL (per 8.5 dBA) | 27,073 / 10,232 | -0.050 (-0.078, -0.021) |
| Aircraft DNL category, | | |
| <45 dBA | 9,968 / 4,086 | Referent |
| 45-49 dBA | 8,451 / 3,041 | 0.009 (-0.031, 0.049) |
| 50-54 dBA | 6,371 / 2,401 | 0.049 (0.006, 0.093) |
| ≥55 dBA | 2,283 / 704 | 0.034 (-0.033, 0.100) |



# Association of noise with odds of incident dementia

| Dementia | Noise measure | N cases / N total | Odds ratio (95% CI) |
|---|---|---|---|
| AD | Community Leq (per 2.8 dBA) | 431 / 2,853 | 1.06 (0.89, 1.25) |
| | Road DNL (per 8.5 dBA) | 437 / 2,918 | 1.17 (0.86, 1.58) |
| | Aircraft DNL category, | | |
| | <45 dBA | 159 / 1,128 | Referent |
| | 45-49 dBA | 124 / 882 | 1.01 (0.65, 1.57) |
| | 50-54 dBA | 104 / 601 | 1.58 (0.93, 2.69) |
| | ≥55 dBA | 50 / 302 | 0.90 (0.59, 1.38) |
| All-cause | Community Leq (per 2.8 dBA) | 458 / 2,853 | 1.06 (0.90, 1.25) |
| | Road DNL (per 8.5 dBA) | 470 / 2,918 | 1.16 (0.86, 1.56) |
| | Aircraft DNL category, | | |
| | <45 dBA | 169 / 1,128 | Referent |
| | 45-49 dBA | 133 / 882 | 1.01 (0.66, 1.56) |
| | 50-54 dBA | 110 / 601 | 1.59 (0.95, 2.65) |
| | ≥55 dBA | 53 / 302 | 0.92 (0.60, 1.39) |



# We are just starting to sound out the potential problem of noise.

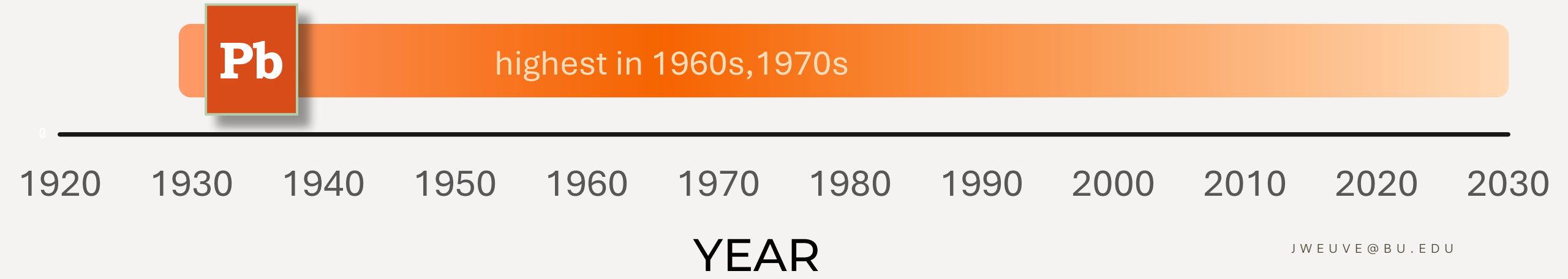
- Noise at **night**, other times
- Noise **spikes**
- **White noise**
- Other noise **sources**
- **Indoor** noise
- Noise vs welcome sound vs **noise policing**

# Expanding the evidence base on the environment in dementia etiology

WHERE TO DIRECT OUR ATTENTION

JWEUVE@BU.EDU

# **Life course:** Period

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# **Life course:** Period

**Air pollution** higher before 2000; composition varies

**Pb** highest in 1960s,1970s

1920 1930 1940 1950 1960 1970 1980 1990 2000 2010 2020 2030

YEAR

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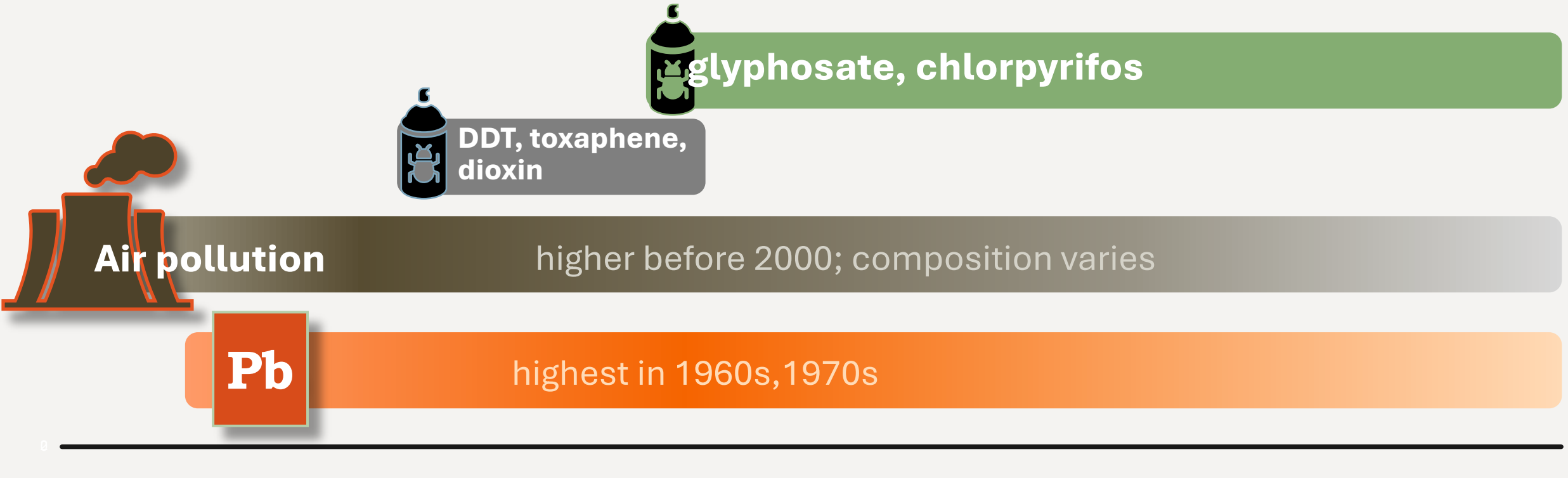
# Life course: Period

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# Life course: Period

Per- and polyfluoroalkyl substances (PFAS)

glyphosate, chlorpyrifos

DDT, toxaphene, dioxin

Air pollution — higher before 2000; composition varies

Pb — highest in 1960s,1970s

1920 1930 1940 1950 1960 1970 1980 1990 2000 2010 2020 2030

YEAR

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# Life course: Period

Extreme weather events

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glyphosate, chlorpyrifos

DDT, toxaphene, dioxin

Air pollution higher before 2000; composition varies

Pb highest in 1960s,1970s

1920 1930 1940 1950 1960 1970 1980 1990 2000 2010 2020 2030

YEAR

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# (*continued*) **Life course:** Life stage / age

**Effects** of some exposures **vary by age**

E.g., Cognitive effects of Pb are stronger in children than in middle-aged adults

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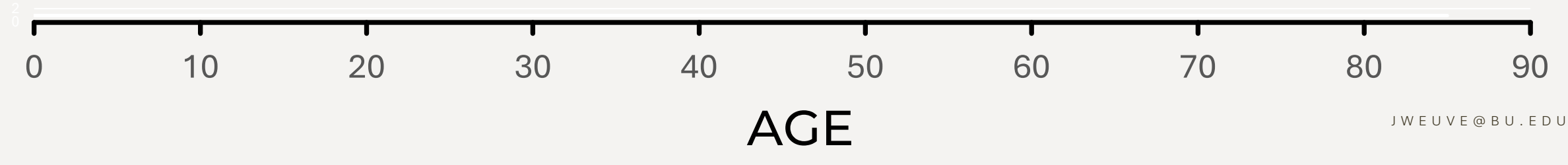
**Age also determines context** of exposure …

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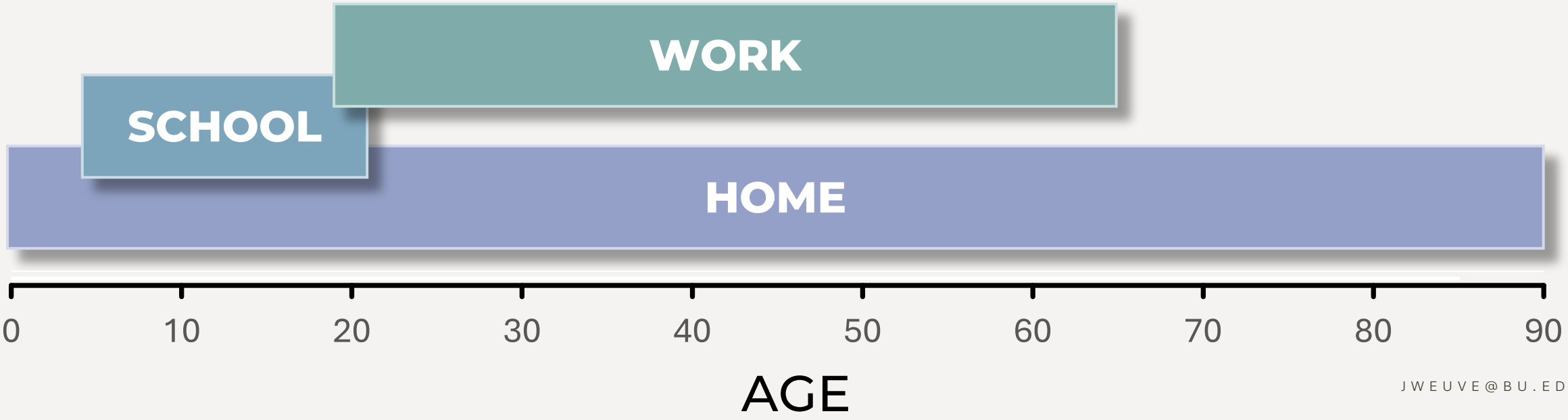


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# Informative complexity

1. Exposure **mixtures**

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# Informative complexity

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2. **Intersection with social/structural** determinants of dementia

   E.g., Race/ethnicity and Environmental Stressors: POtential drivers of Dementia and stroke inequities (RESPOnD). PI: Marcia Pescador Jimenez (R01NS139186)

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GECC | GATEWAY EXPOSOME COORDINATING CENTER

Advancing life-course research on the AD/ADRD exposome

Learn more at www.gatewayexposome.org

An NIA-funded initiative to advance life-course research on the AD/ADRD **exposome** (U24AG088894)

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R01AG067497
R01AG065359
R01ES028694
R01ES029509
Alz Assn NIRG-396139
R01AG11101


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# Some dirt might hurt

## *why the* **environment** *merits attention as a contributor to* **dementia risk**

JENNIFER WEUVE, MPH, SCD

MAY 2025

BOSTON UNIVERSITY SCHOOL of Public Health

# Land Acknowledgment

The territory on which Boston University stands is that of **The Wampanoag** and **The Massachusett People**. BU's campuses are places to honor and respect the history and continued efforts of the Native and Indigenous community leaders which make up Eastern Massachusetts and the surrounding region.

This statement is one small step in acknowledging the history that brought us to reside on the land, and to help us seek understanding of our place within that history. **Ownership of land is itself a colonial concept; many tribes had seasonal relationships with the land we currently inhabit.** Today, **Boston is still home to indigenous peoples**, including the Mashpee Wampanoag and Wampanoag Tribe of Gay Head (Aquinnah).

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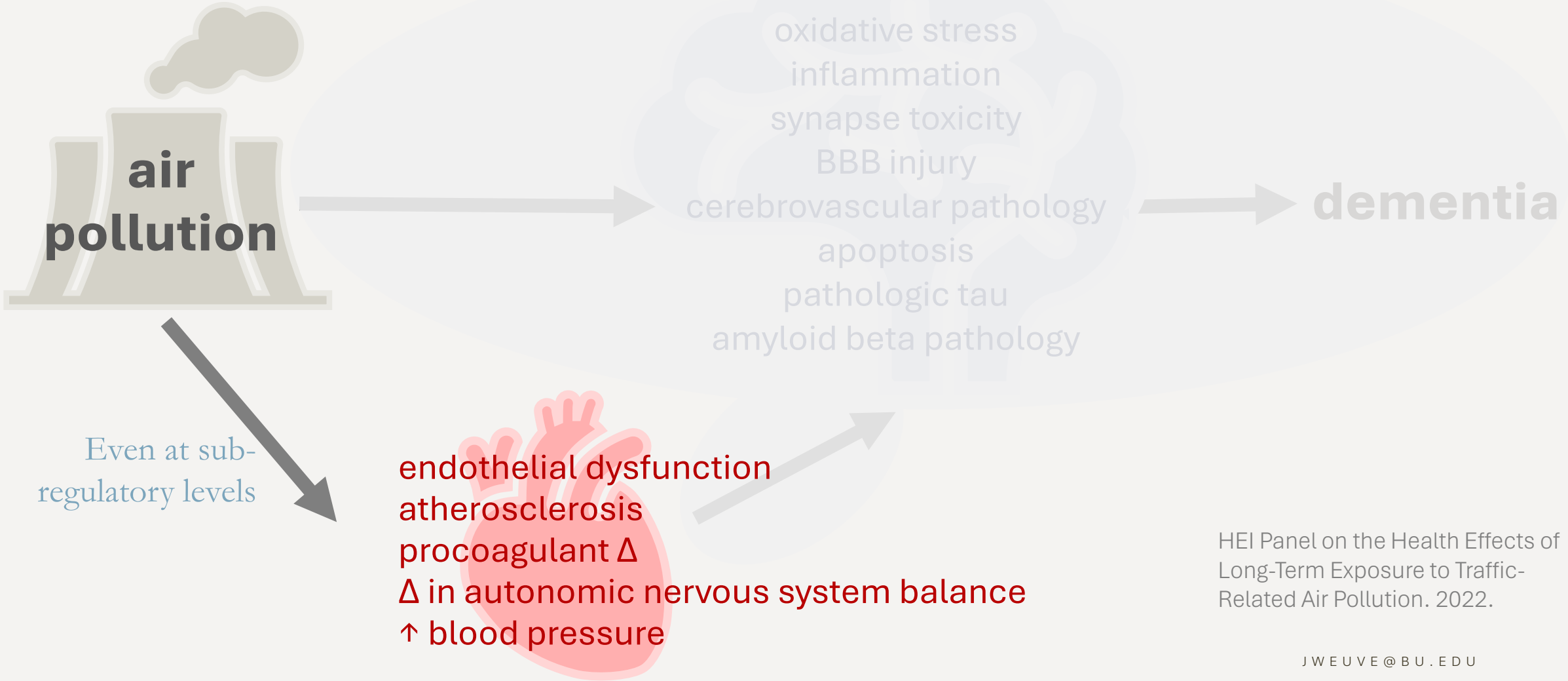
# Air pollution's cardiotoxicity is well-established.




HEI Panel on the Health Effects of Long-Term Exposure to Traffic-Related Air Pollution. 2022.

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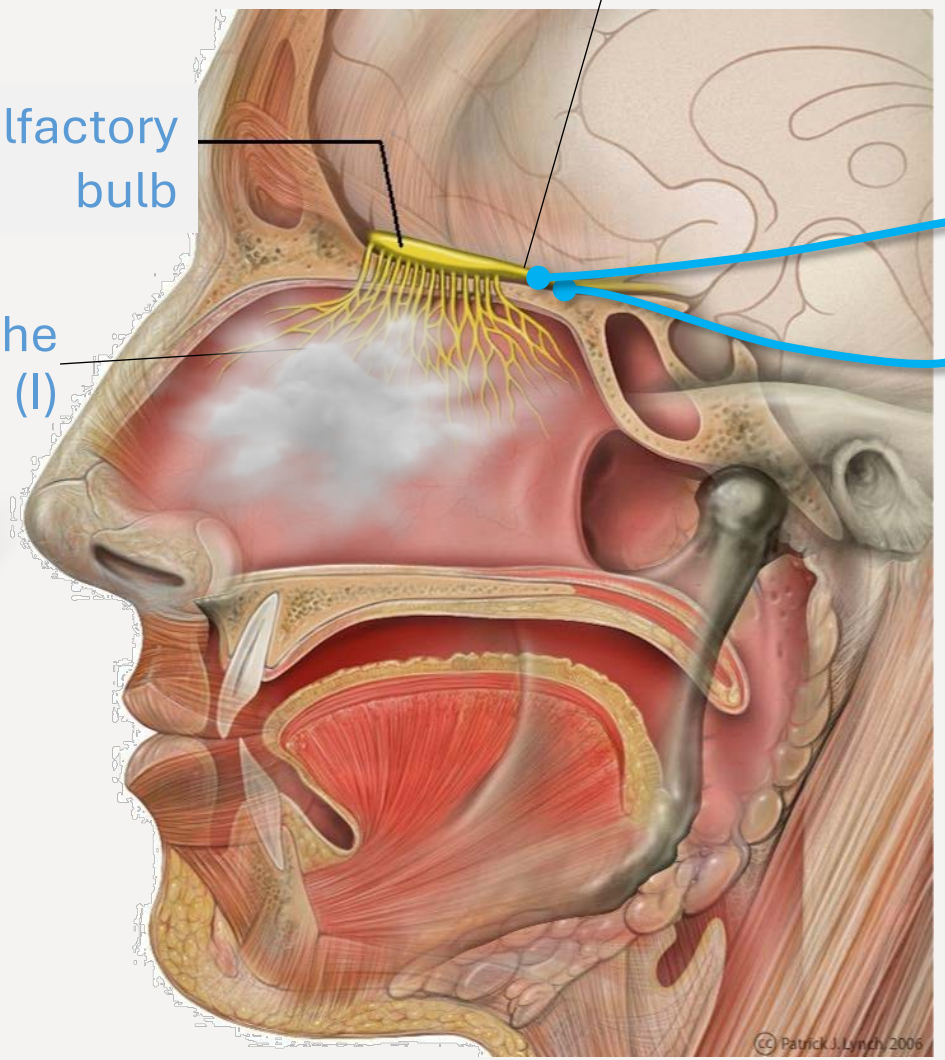
# It might also act more directly by accessing the brain from the lungs via circulation, or …




Via **int** **athway**

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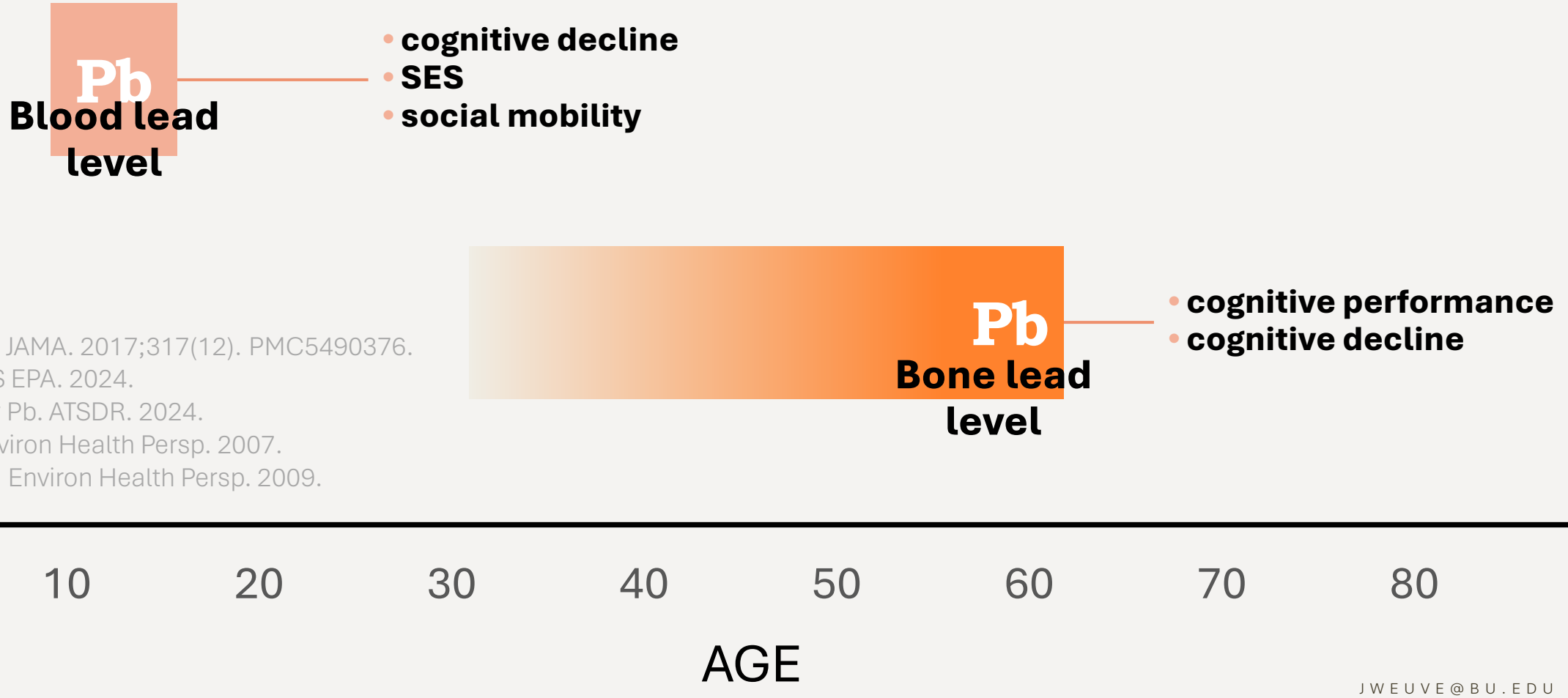
# The evidence unequivocally supports the adverse effects of Pb on neurodevelopment. In addition …





Reuben et al. JAMA. 2017;317(12). PMC5490376.
ISA for Pb. US EPA. 2024.
Tox Profile for Pb. ATSDR. 2024.
Shih et al. Environ Health Persp. 2007.
Weuve et al. . Environ Health Persp. 2009.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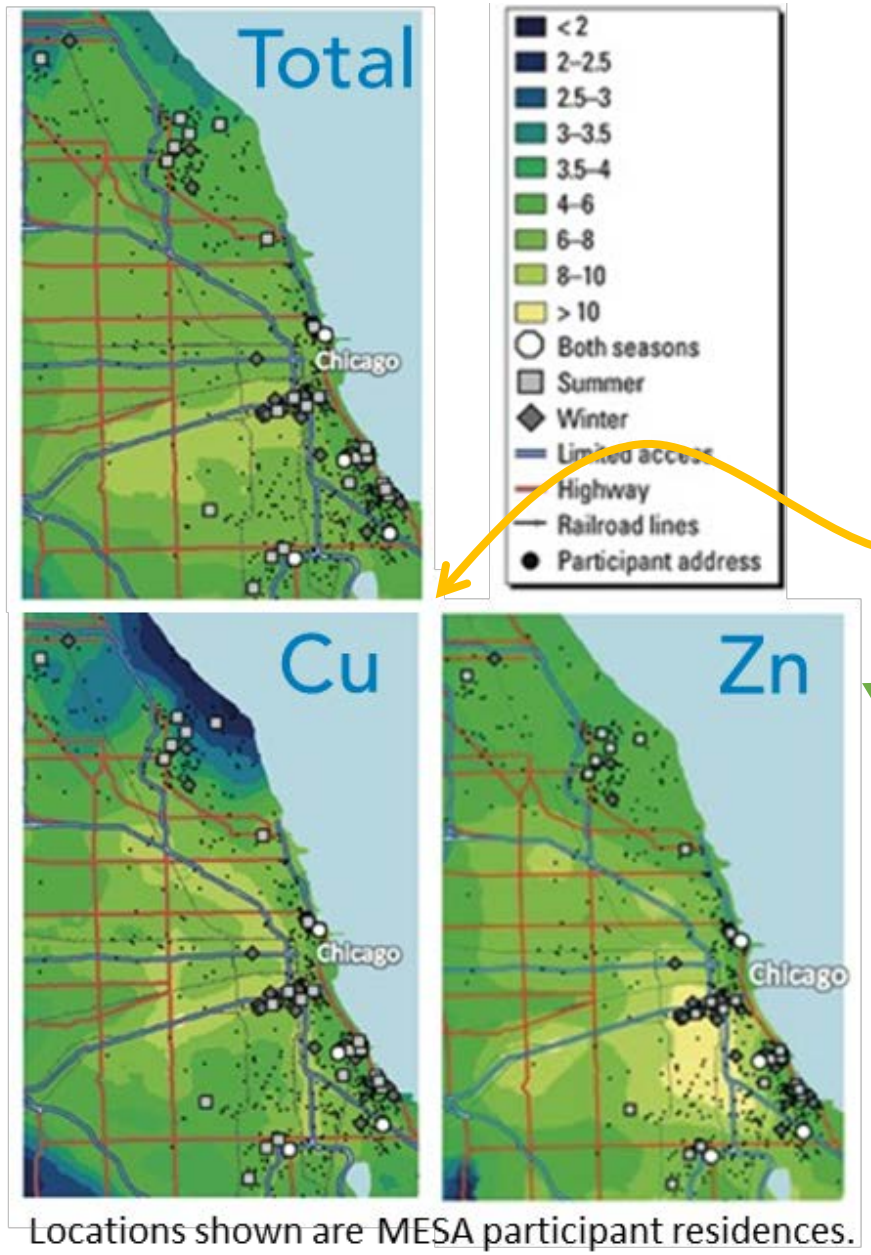



Locations shown are MESA participant residences.

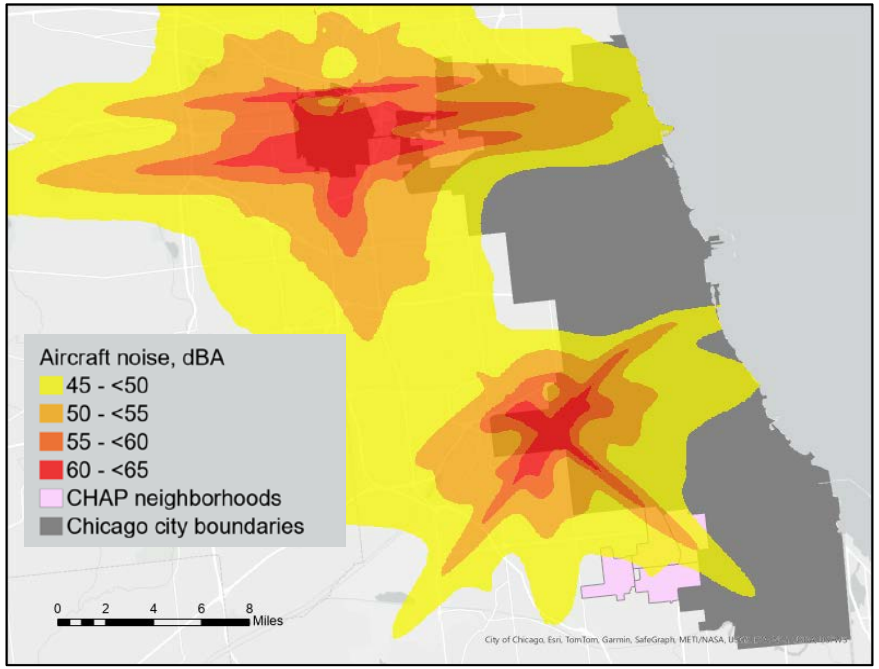
Zhang et al. *Environ Health Perspect. 2014.*

Predicted concentrations (ng/m$^3$), in the Chicago metro area, of

1. total coarse PM
2. coarse PM Cu, and
3. coarse PM Zn

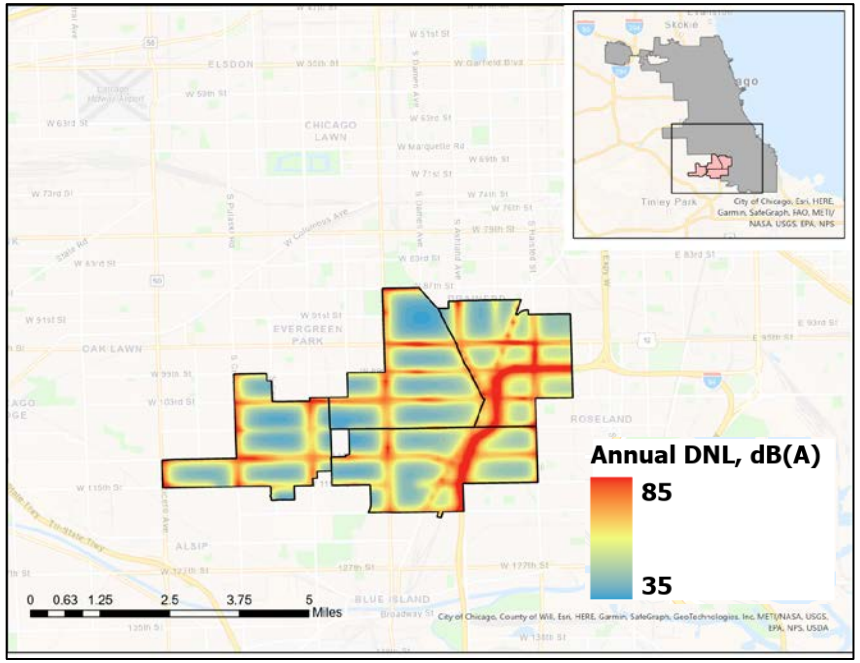
# Noise in metro Chicago and the CHAP area

## Aircraft



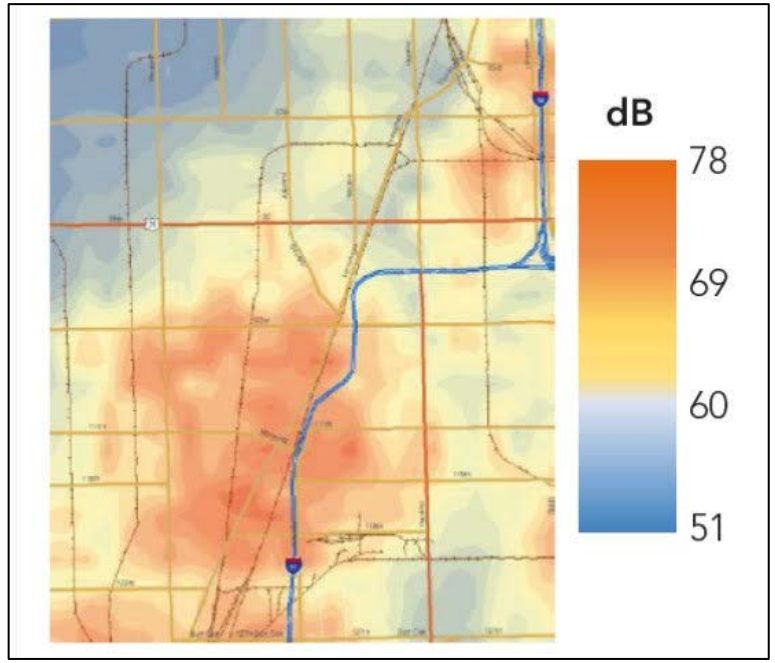

Aircraft noise for CHAP area, 2016, from publicly available DOT

## Road




Road noise for CHAP area, 2010

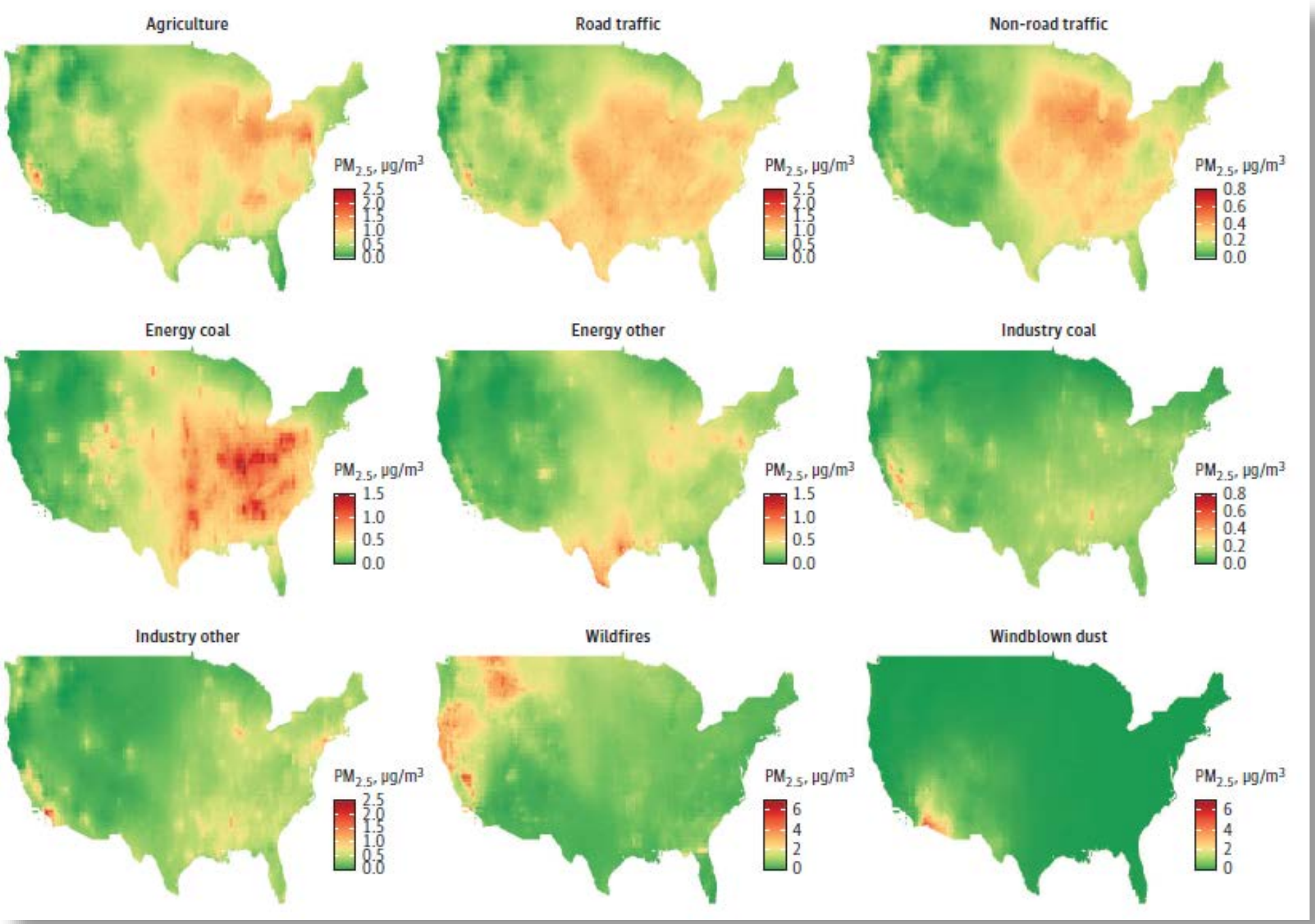
## Community




Community noise for subsection of CHAP area, 2006-2007

Grady et al. In preparation.
R01AG065359

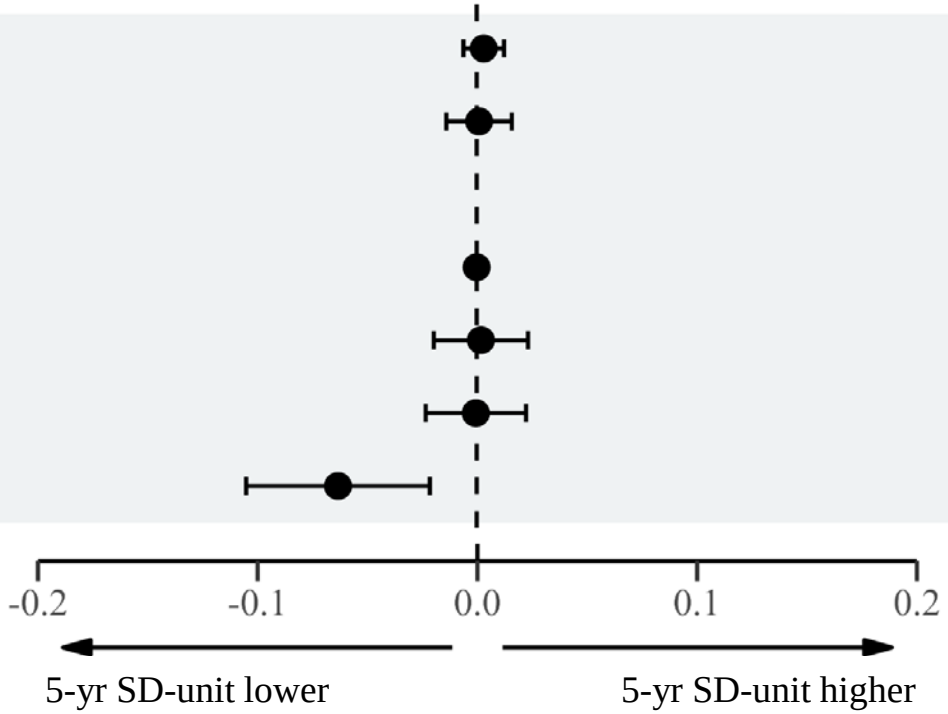
The spatial distribution of source-specific fine particulate matter ($PM_{2.5}$) across the US, 2017




Zhang et al. JAMA Int Med 2023

# Association of noise with rate of change in cognitive performance

| Noise measure | N obs / N participants | Difference in 5-yr change, SD-units (95% CI) |
|---|---|---|
| Community Leq (per 2.8 dBA) | 27,003 / 10,204 | 0.003 (-0.006, 0.012) |
| Road DNL (per 8.5 dBA) | 27,073 / 10,232 | 0.001 (-0.014, 0.016) |
| Aircraft DNL category, | | |
| <45 dBA | 9,968 / 4,086 | Referent |
| 45-49 dBA | 8,451 / 3,041 | 0.002 (-0.019, 0.023) |
| 50-54 dBA | 6,371 / 2,401 | 0.0004 (-0.0232, 0.0225) |
| ≥55 dBA | 2,283 / 704 | -0.063 (-0.105, -0.021) |



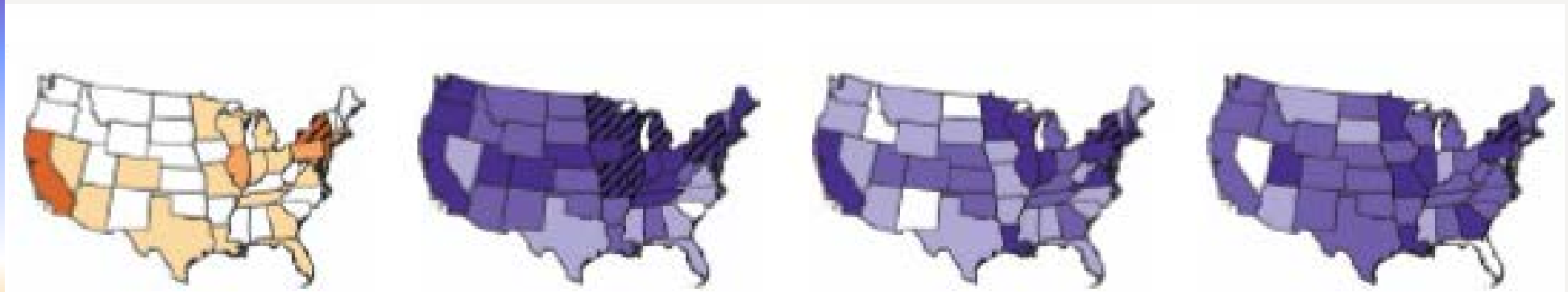
# 3. *Environmental injustice* over the life course may be a critical source of racial and ethnic inequities in dementia.

$NO_2$

**Higher** than state average $NO_2$ concentration

**Lower** than state average $NO_2$ concentration

(2010)



Non-Hispanic White

Non-Hispanic Black

Hispanic

Non-Hispanic Asian

Liu et al. Environ Health Perspect. 2021;129(12). PMC8672803.

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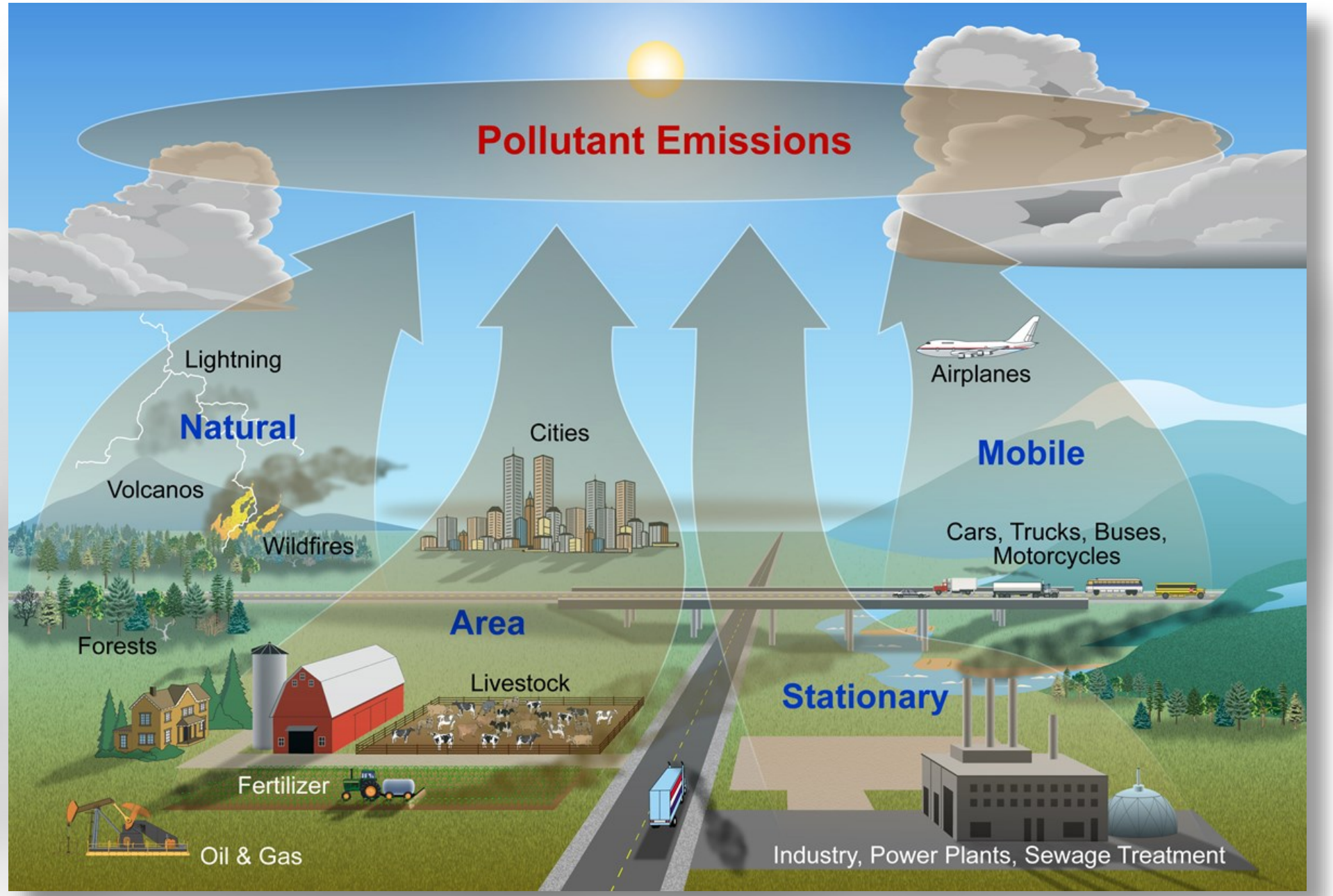
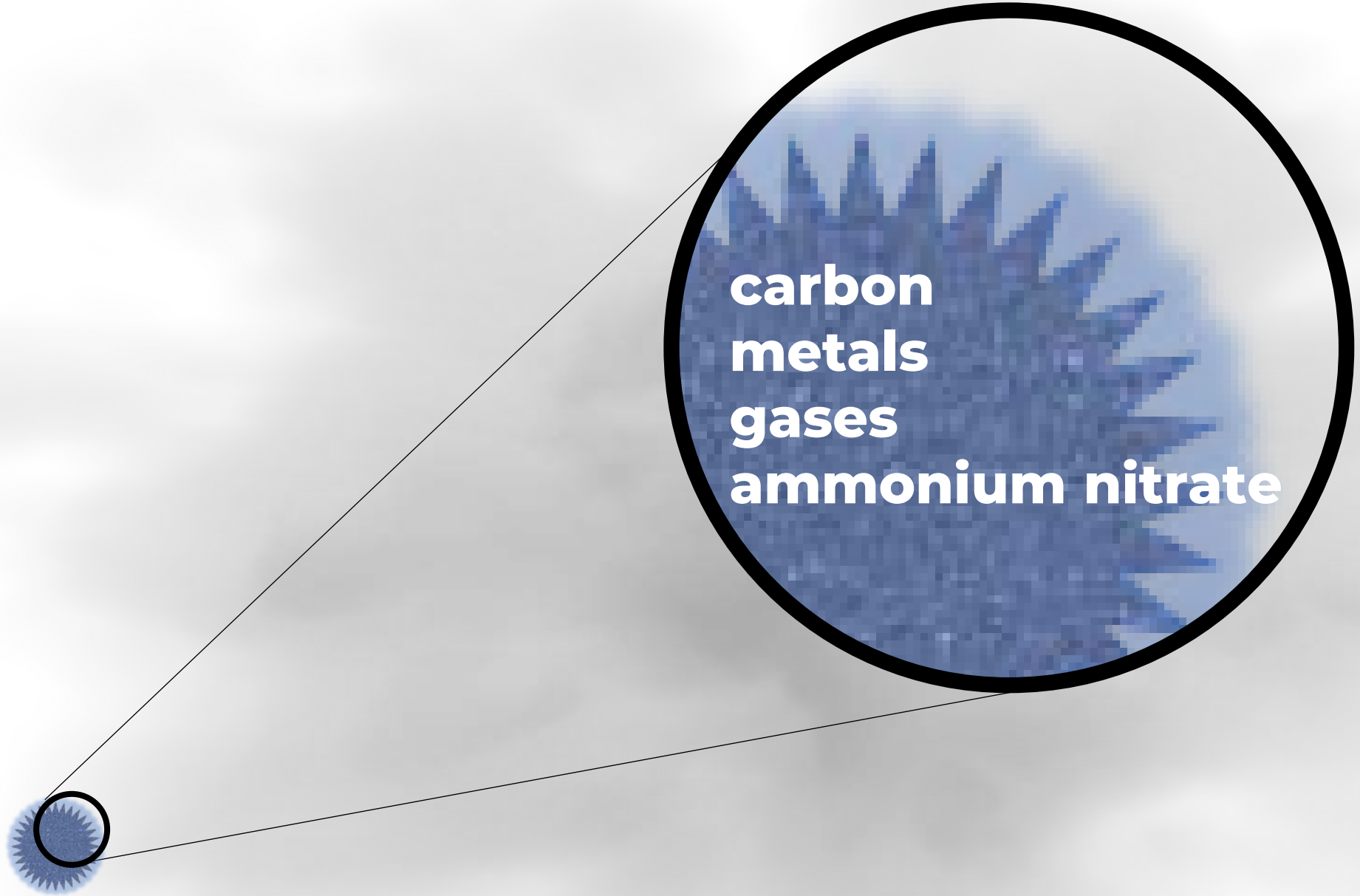



National Park Service

# How might exposure to air pollution influence dementia etiology?




Jennifer Weuve, ScD jweuve@bu.edu

# US EPA Integrated Science Assessment for PM (2019)

## SCOPE

$PM_{10}$
$PM_{10-2.5}$
$PM_{2.5}$
Ultrafine PM

All health outcomes, children + adults

100s of animal and human studies

## CONCLUSION

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)

## SCOPE

$PM_{10}$
$PM_{10-2.5}$
$PM_{2.5}$
$NO_2$
$NO_x$
$O_3$
BC
Traffic proximity

Cognition
Cognitive decline
Dementia
MRI

66 studies
(adults, mostly 65+)

## CONCLUSIONS

35 studies met quality review.

$PM_{2.5}$ → faster decline.

Other evidence mixed or sparse.

# Systematic review: Wilker et al. *BMJ* (2023)

## SCOPE

| | | |
|---|---|---|
| $PM_{10}$ | $NO_2$ | BC |
| $PM_{10-2.5}$ | $NO_x$ | Traffic proximity |
| $PM_{2.5}$ | $O_3$ | Other |

Dementia

51 studies (adults, mostly 65+)

## CONCLUSIONS

16 studies in meta-analysis, of which 11 deemed high risk of bias

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

Evidence re: other pollutants mixed or sparse.

# Other dimensions of time

1. **Duration** of exogenous exposure.
   - How long exposure was present in a person's environment: weeks vs years

2. **Residence time** in the body.
   - Pb, Cd, and persistent organic pollutants (POPs) remain in the body for years and decades
   - Possibility: continued exposure to and effects of these chemicals

3. **Persistence of effect** caused by an exposure. E.g.,
   - Epigenetic programming
   - Educational attainment

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