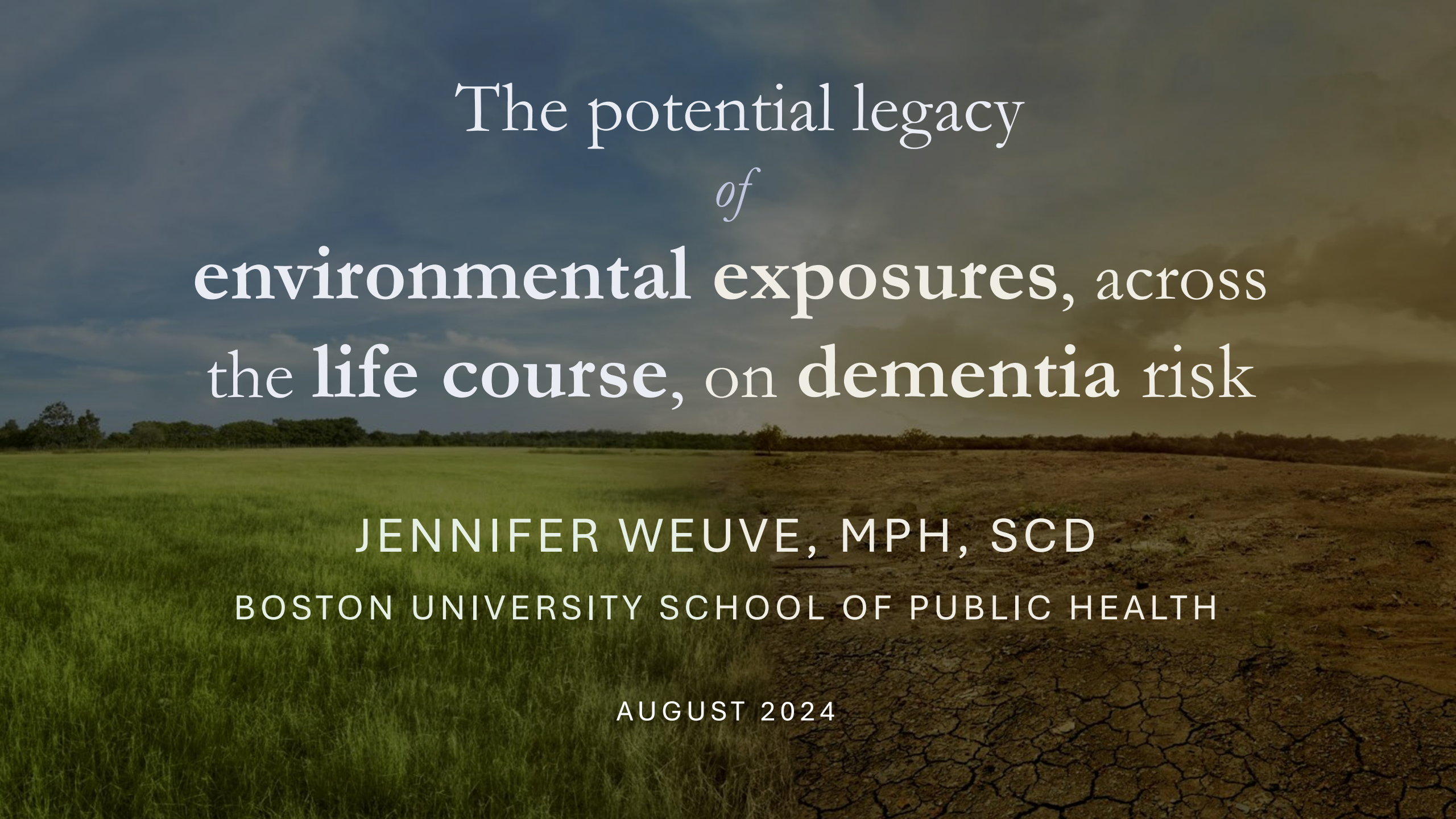

The potential legacy *of* **environmental exposures**, across the **life course**, on **dementia** risk

JENNIFER WEUVE, MPH, SCD

BOSTON UNIVERSITY SCHOOL OF PUBLIC HEALTH

AUGUST 2024

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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“Environmental exposure”

persistent organic pollutants

PCBs, PFAS, dioxins, DDT

heavy metals

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

- 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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Why should environmental exposures across the life course **merit our attention** for understanding dementia risk?

4 INTERCONNECTED REASONS …

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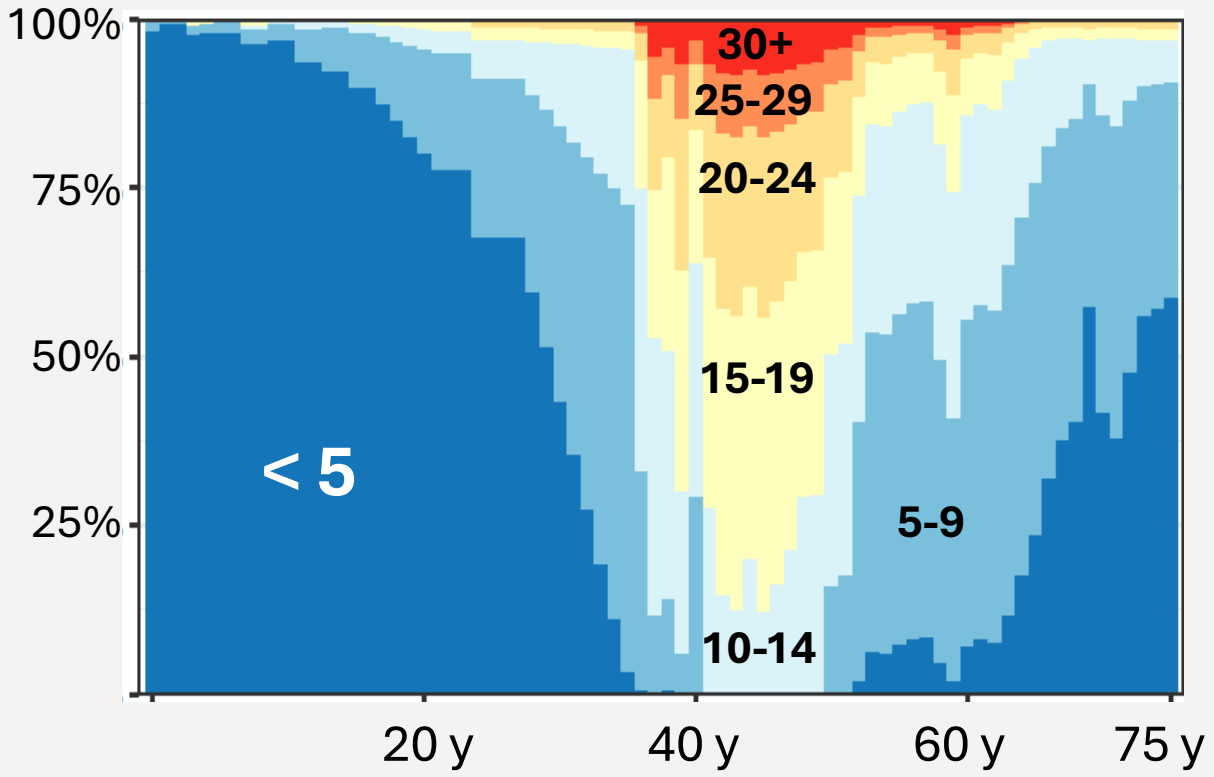
1. Exposures to *known neurotoxicants*, are or were *common* among children and middle-aged adults.

% 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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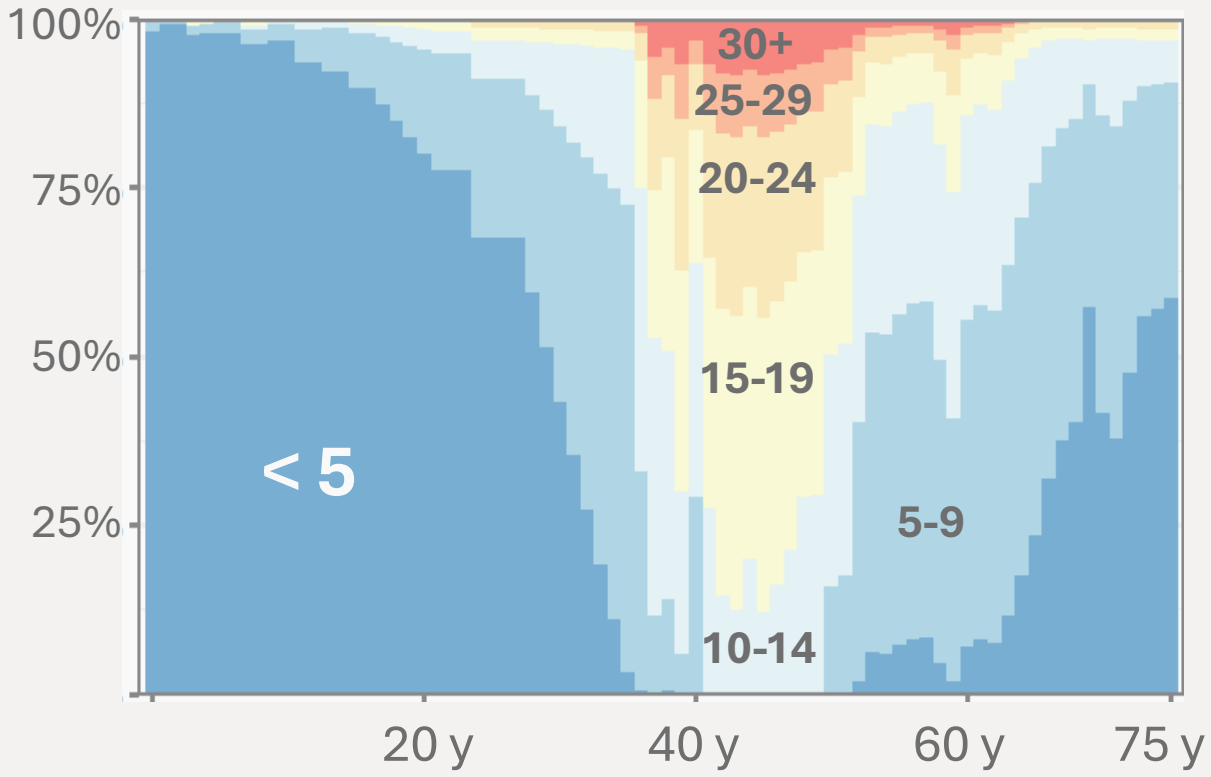

McFarland, et al. Proc Natl Acad Sci U S A. 2022;119(11). PMC8931364.

PESTICIDES

Most children exposed at home

1.8 billion agricultural workers globally; most are exposed

War-related exposure

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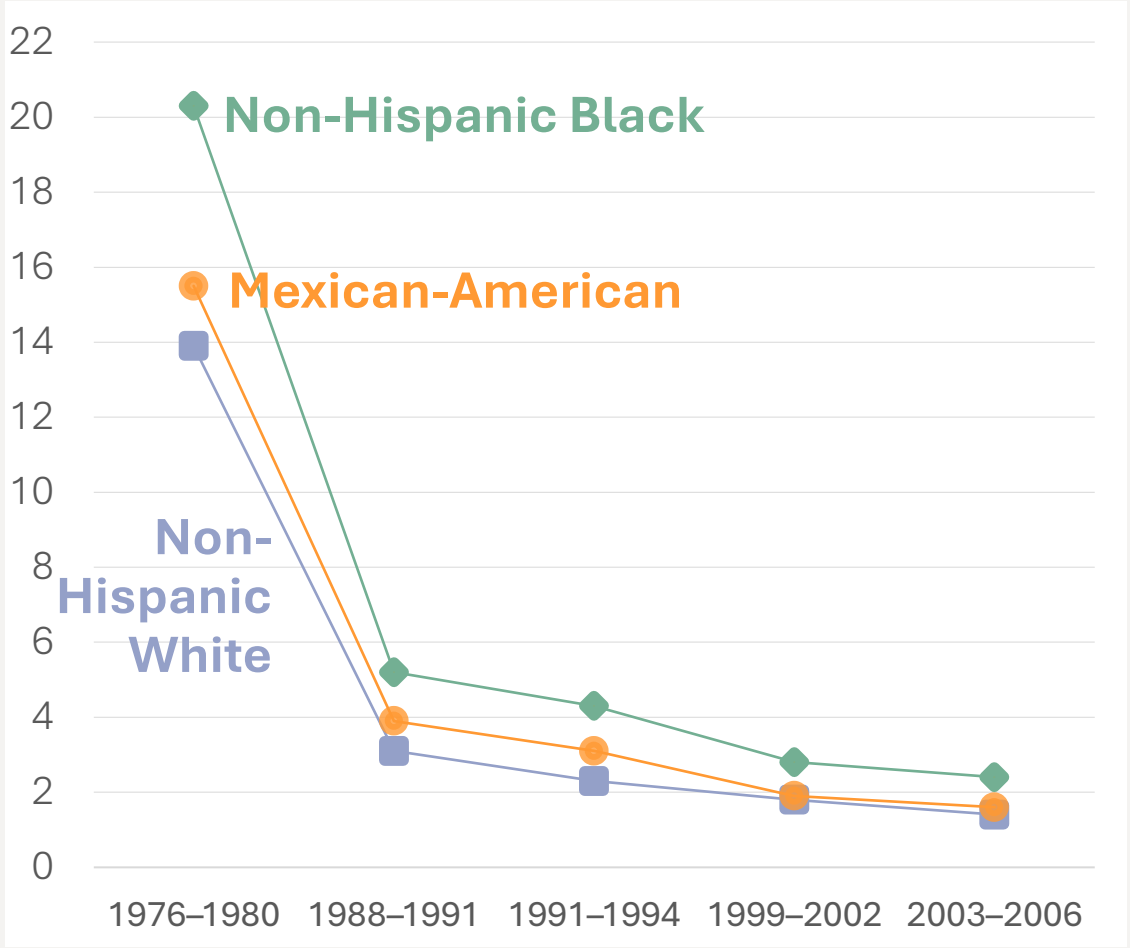
2. *Environmental injustice* over the life course may be a critical source of racial and ethnic inequities in dementia.

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



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

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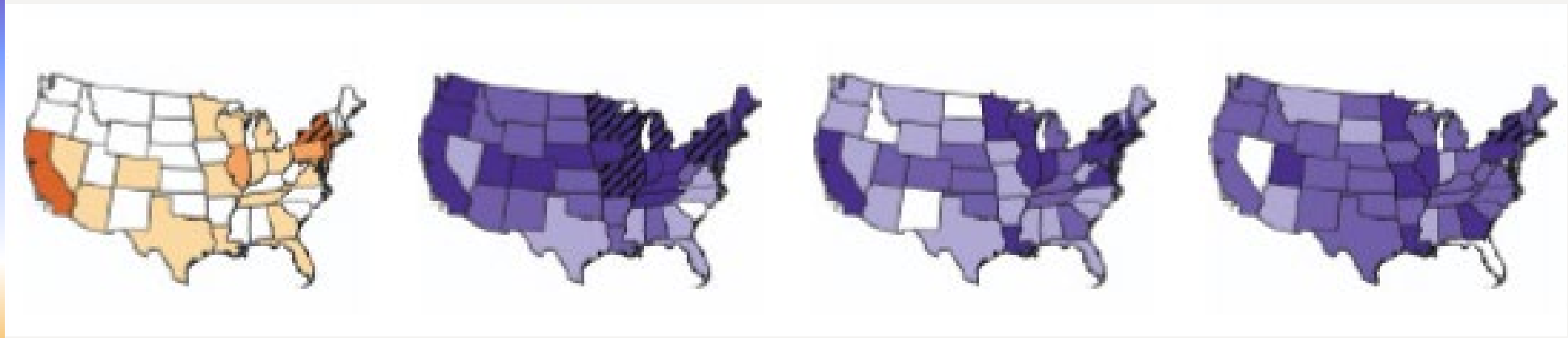
2. *Environmental injustice* over the life course may be a critical source of racial and ethnic inequities in dementia.

NO_2

Higher than average NO_2 concentration

Lower than 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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3. We do not know how to intervene on dementia-promoting *exposures that lie in the past.*

Yet such past exposures are common (see #1).

Also consider **acute environmental events**

- 2005: **700,000** acutely affected by **Hurricane Katrina**
- 2023: **2.5 million displaced** by tornadoes, wildfires, hurricanes, and other **disasters**

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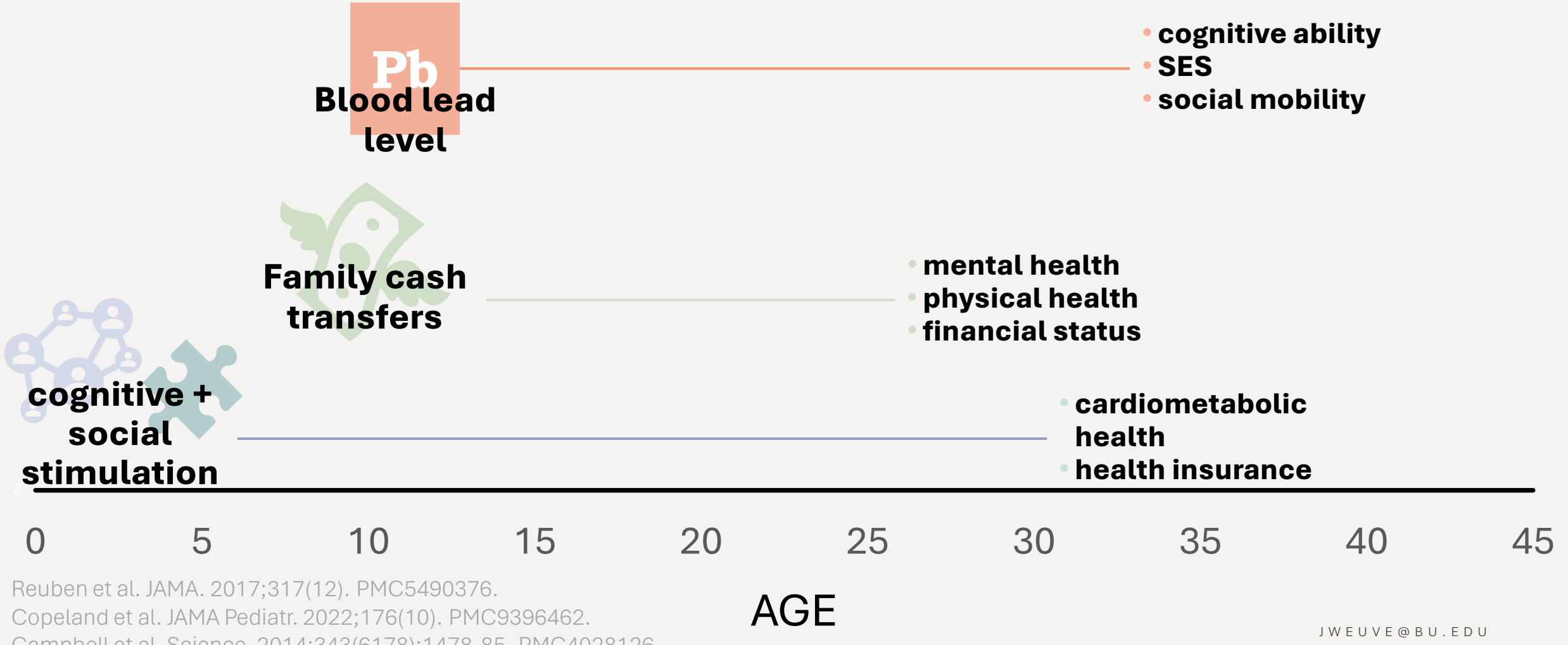
4. *Untapped potential* for large impact on the public health burden of dementia.



Reuben et al. JAMA. 2017;317(12). PMC5490376.
Copeland et al. JAMA Pediatr. 2022;176(10). PMC9396462.
Campbell et al. Science. 2014;343(6178):1478-85. PMC4028126.

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The timing dimensions

OF ENVIRONMENTAL EXPOSURES

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Period (year)

Extreme weather events

Per- and polyfluoroalkyl substances (PFAS)

glyphosate, chlorpyrifos

DDT, toxaphene, dioxin

Air pollution higher before 2000; composition varies

Pb highest in 1960s,1970s

0

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

YEAR

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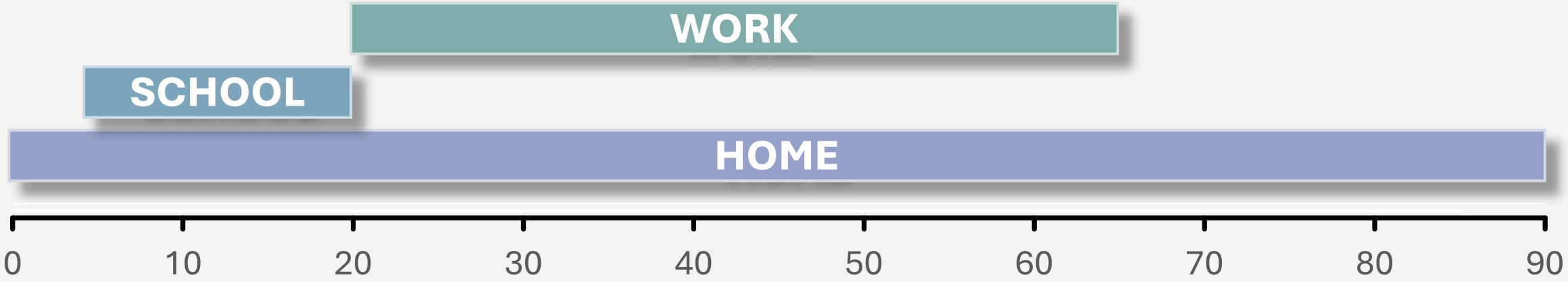
Life stage (age)

Effects of some exposures **vary by age**

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

Age determines context of exposure …

Each of these takes on gendered, racialized, and ethnicized forms that vary by period and socioeconomic status



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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Critical challenges

IN GENERATING USEFUL EVIDENCE ON THE EFFECTS OF LIFE COURSE ENVIRONMENTAL EXPOSURES ON DEMENTIA RISK

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Challenge 1: Asking *good questions* …

Which exposure during which life stage matters most?

What fraction of **dementia cases in this birth cohort can be attributed to exposure** during this life stage?

When is it best to intervene – and how?

- What if the exposure lies squarely in the past?

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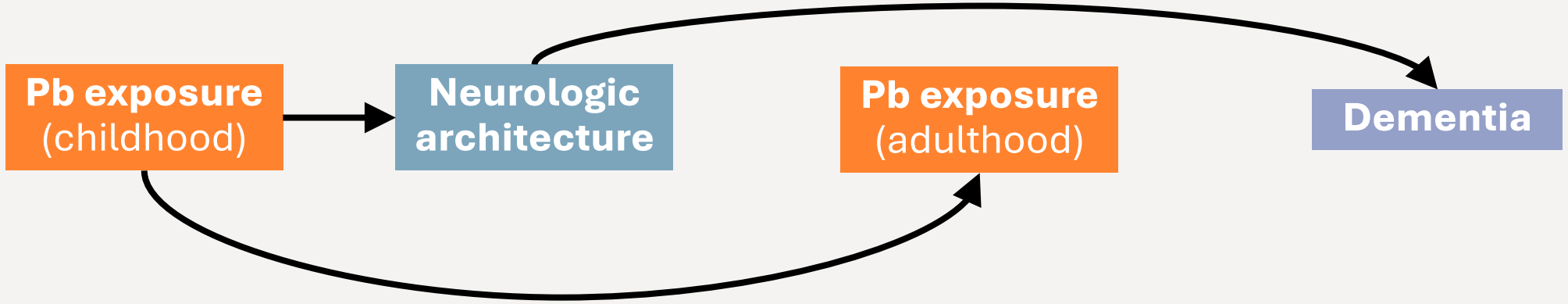
… and aligning them with *methods to answer them:*

applying life course frameworks to inform useful questions and evidence

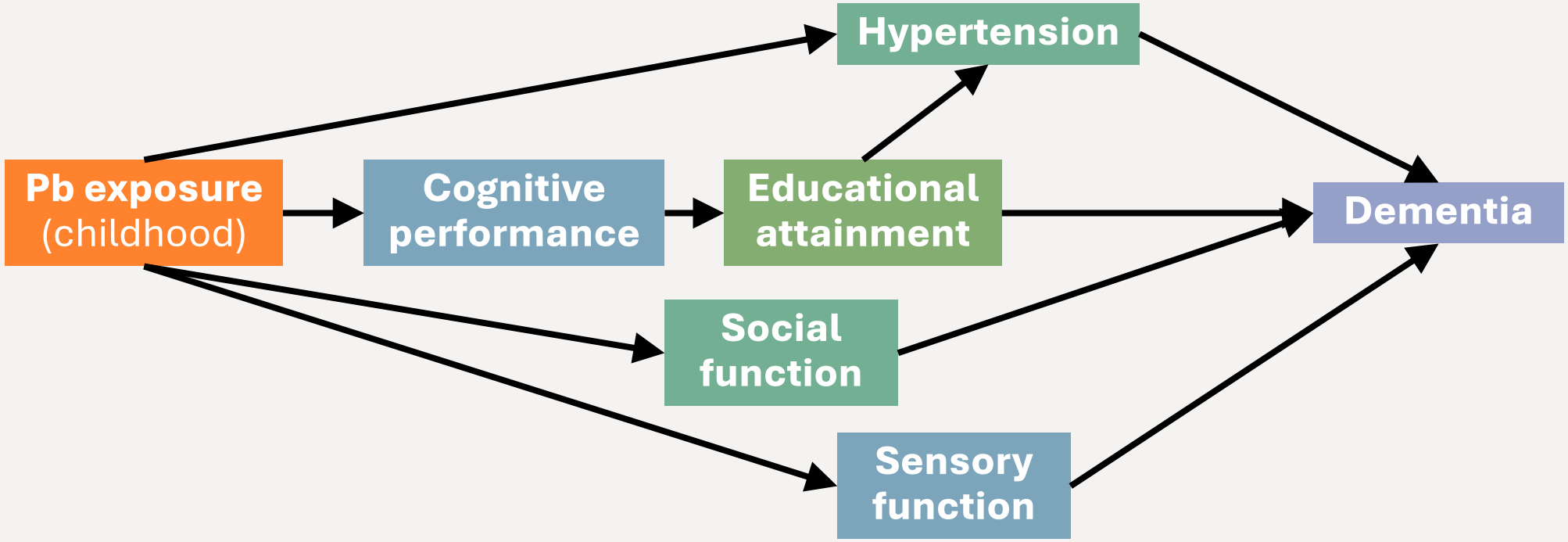
"Sticky" Trajectory/Pathway/Chain of events

"Sensitive/Critical period/Latency



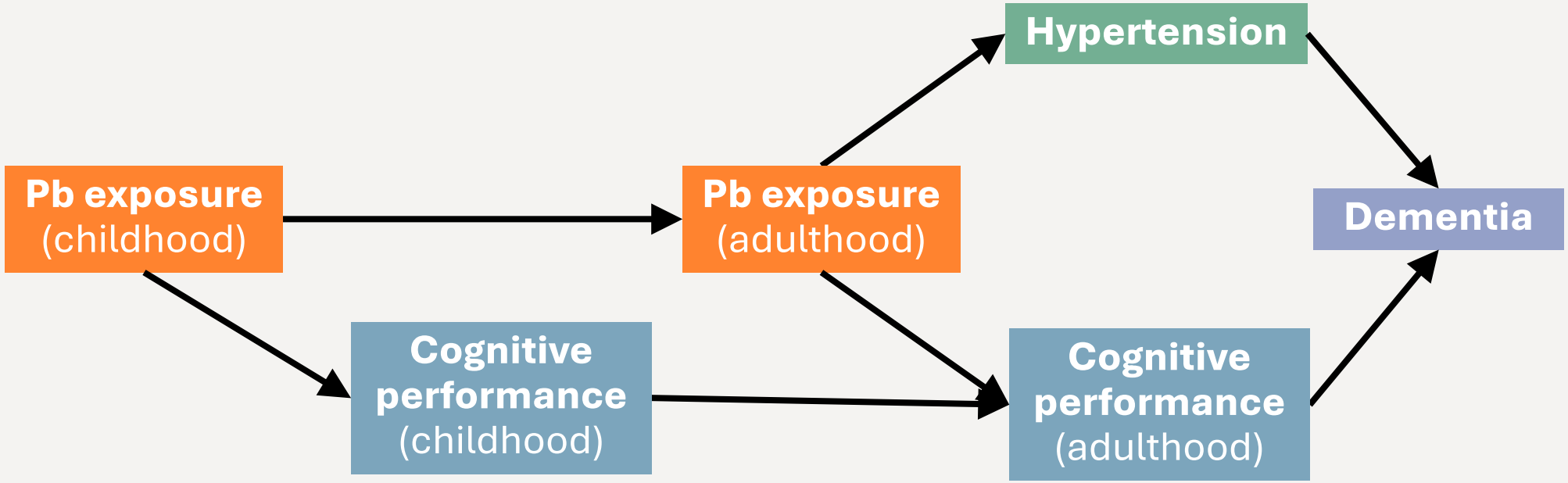
… applying life course frameworks to inform useful questions and evidence (continued)

Cumulative risk: multiple cascades *from a single period of exposure*

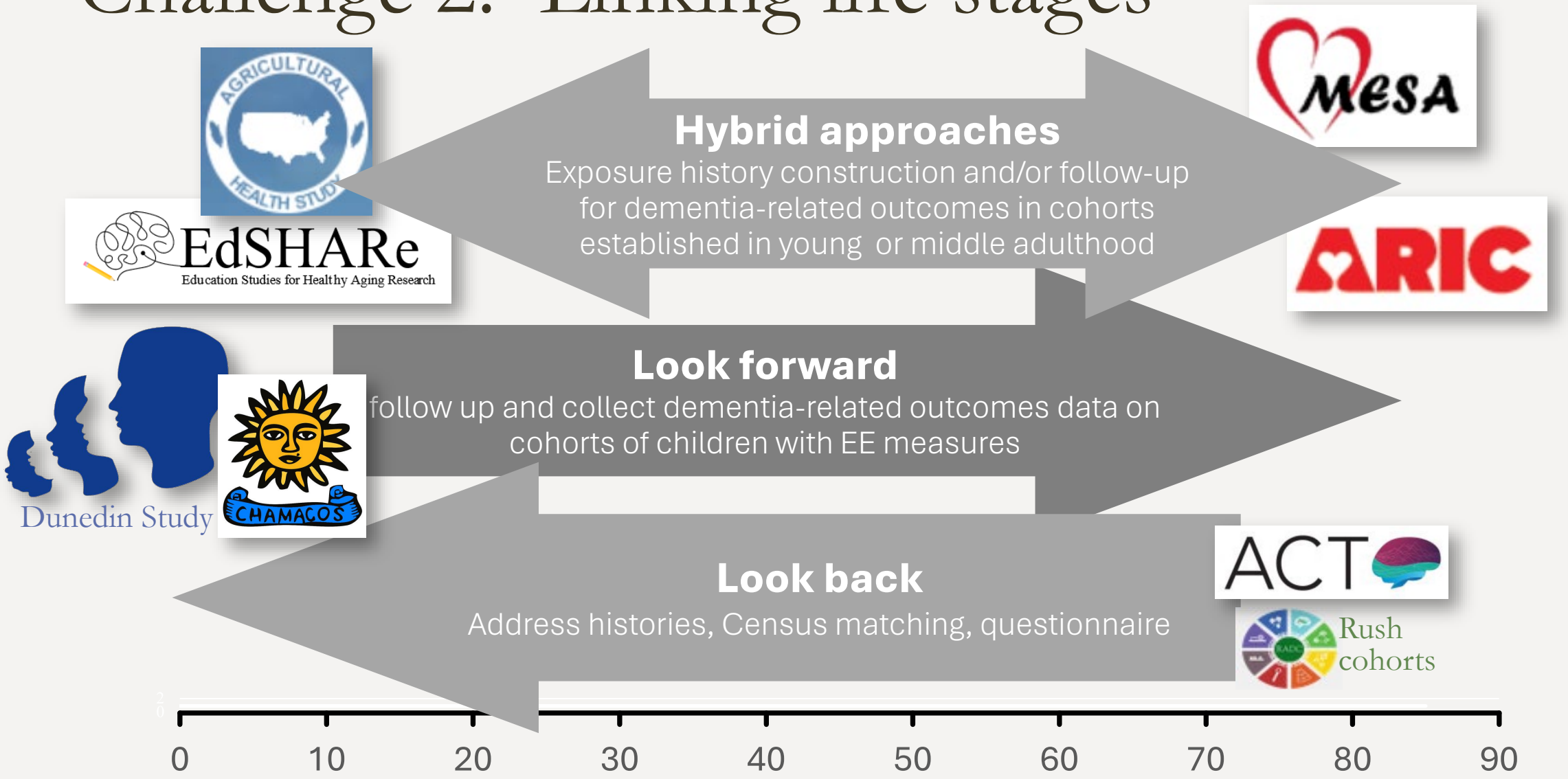


… applying life course frameworks to inform useful questions and evidence (continued)

Cumulative risk: cascades *from repeated exposure*



Challenge 2: Linking life stages



Challenge 3: Measurement quality

	USEFUL FOR/WHEN/GIVEN …	BUT WATCH OUT FOR …
BIOMARKERS	• **Integrating exposure** from multiple sources • Specific chemical of interest has a known toxicokinetic profile	▪ **Specificity to time period** (e.g., blood vs bone) ▪ Expense or logistical challenges ▪ **Physiologic interference** (e.g., renal function)
SPATIOTEMPORAL MEASURES	• Specificity to period • Address data are on file, **even if persons are deceased**	▪ **Errors in person location** (where people spent their time) ▪ Assumptions about transfer to person
POLICY MEASURES	• Potential for **natural experiment**	▪ Not an option for all exposures ▪ Assumptions in analyses
OCCUPATIONAL MEASURES	• **1/3 of adulthood** time is spent working • Job-exposure matrices are available	▪ **Complexity** that is potentially informative ▪ Confounding by employment status

Challenge 4: Embracing informative complexity

1. Exposure **mixtures/exposome**

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)

Recommendations for advancing the evidence

1. Support the development of **methods to reconstruct environmental exposure histories**. Includes support for secure methods for strategic but wider data-sharing.
2. Support the **follow-up of younger cohorts into older age**, especially cohorts that have been characterized in terms of their environmental exposures.
3. Promote research on **intervening on effects of exposures that have ended**.
4. Promote this research as **an essential pursuit toward reducing racial and socioeconomic inequities** in dementia.
5. Foster **deep multi- and trans-disciplinary collaborations** that can build capacity for rigorous life course research on environmental exposures and dementia risk. Include historians! Policy experts!
6. Value the **evolution of methods toward more rigor** over immediate perfection.

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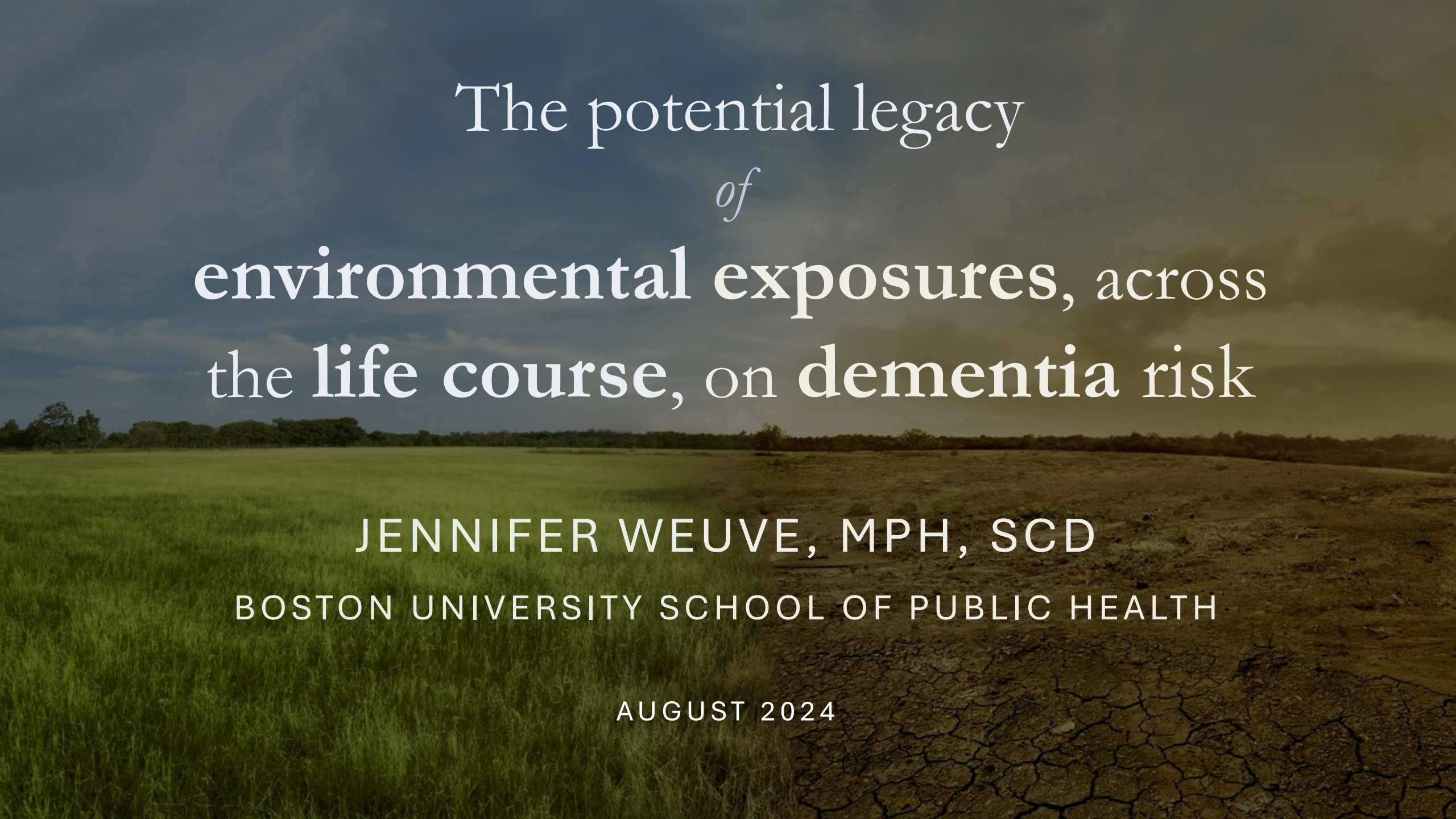

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