

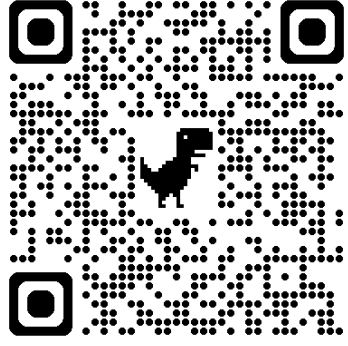
Does Duration and Timing of Exposure Matter?

Interactions Between PM_{2.5} And APOE ε4 in Later-life Cognitive Decline

P1-15

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 Questions?
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1. PM_{2.5} accelerates cognitive decline among ε4 carriers through cumulative and timing-specific exposure pathways.
2. Sustained PM_{2.5} burden may trigger the ε4-associated neuropathology cascade. Exposure during the 60s emerges as a sensitive window when compensatory neural mechanisms weaken before genetic-related neuropathology becomes more prominent in late older adulthood.

INTRODUCTION

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RESULTS

Figure 1. Cognitive Trajectory by Duration of PM_{2.5} Exposure and APOE ε4 Carrier Status.

Figure 2. Cognitive Trajectory by Timing of PM_{2.5} Exposure and APOE ε4 Carrier Status.

DISCUSSION

ACKNOWLEDGMENT

Motivation

- APOE* ε4 carriers may be particularly **vulnerable to PM_{2.5}-related neurotoxicity** due to impaired amyloid-β clearance and heightened neuroinflammatory responses.
- There is supportive evidence of genetic susceptibility to PM_{2.5} in animal models, but **findings in human populations remain inconsistent**.
- Few prior studies considered **the role of duration and timing of PM_{2.5} exposure**.

Study Objectives

- To determine whether PM_{2.5} accelerates cognitive decline differently by *APOE* ε4 status in U.S. older adults using different timing exposure models.

✓ **Accumulation-of-risk model:** Cumulative PM_{2.5} burden may better capture biological damage that unfolds over time and reveal stronger differences between ε4 carriers and non-carriers.

✓ **Sensitive-window model:** Exposure during specific life stages may be more consequential as compensatory capacity and the biologic effects of *APOE* ε4 change across later adulthood.

Data/Sample

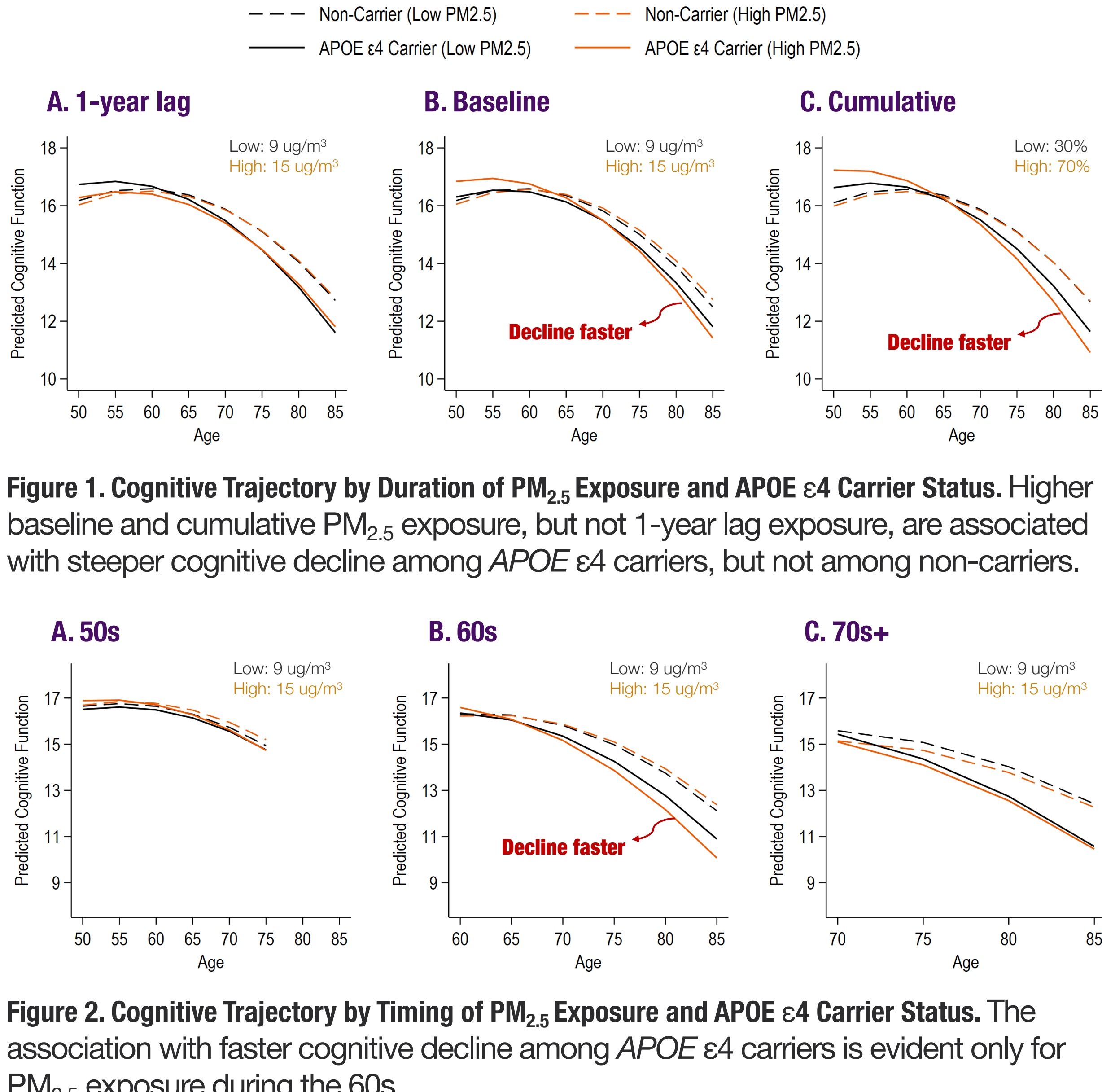
- U.S. Health and Retirement Study (2002-2018) linked to census-tract annual PM_{2.5} data from the Contextual Data Resource
- Community-dwelling adults aged 50–85 at baseline with *APOE* genotype data and ≥ 1 cognitive assessment (N = 18,318)

Measures

- Cognitive function:** Modified Telephone Interview for Cognitive Status score, 0–27
- APOE* ε4:** Non-carriers vs. ε4 allele carriers
- PM_{2.5} exposure:**
 - 1-year lag** Year before each assessment
 - Baseline** Year before baseline assessment
 - Cumulative** % years >12 μg/m³
 - Life-stage** Mean in the 50s, 60s, and 70+
- Covariates:** Sociodemographics, *APOE* imputation status, chronic conditions, survey wave, and attrition-related indicators

Analysis

- Three-level growth curve models estimated cognitive trajectories across age, with repeated assessments within individuals, nested within census tracts
- Estimated interaction effects: PM_{2.5} × *APOE* ε4 for cognitive level; PM_{2.5} × *APOE* ε4 × age for rates of cognitive decline



- Cumulative PM_{2.5} exposure may repeatedly activate **stress-related APOE expression and inflammatory responses** among ε4 carriers, accelerating cognitive decline.
- 1-year exposure may have transient effects.
- Exposure during the 60s may represent a **sensitive window** when PM_{2.5} accelerates ε4-related neurodegenerative processes.
- Null findings in the 50s may reflect delayed effects or vulnerability that is not yet phenotypically apparent.
- Null findings at ages 70+ may reflect dominant ε4-driven decline at older ages, or selective survival and attrition.

ACKNOWLEDGMENT

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