

Neighborhood Deprivation and the Risk of Young-Onset Dementia and Its Subtypes

An Analysis of the All of Us Research Program

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KEY FINDING

Living in the most deprived neighborhoods was linked to **44% higher young-onset dementia risk** and **nearly double the risk of young-onset Alzheimer's disease**, independent of genetic risk.

BACKGROUND

- Young-onset dementia (YOD, onset before age 65) affects more than 200,000 Americans, yet non-genetic risk factors remain poorly defined.
- Neighborhood socioeconomic deprivation is a known correlate of late-life dementia, but its role in YOD is unclear.

OBJECTIVE

- Determine whether higher neighborhood deprivation increases the risk of YOD and its subtypes in a large, diverse U.S. cohort.

METHODS

- Design:** Retrospective cohort study, All of Us Research Program.
- Sample:** 180,549 adults under age 60, dementia-free at enrollment (2017 to 2022); mean follow-up 33 months.
- Exposure:** Neighborhood Deprivation Index (NDI), a census block-group composite of poverty, education, income, employment, and housing, analyzed in quintiles (Q1 least to Q5 most deprived).
- Outcome:** Incident YOD (ICD-9/10) before age 65: all-cause, Alzheimer's disease, and vascular dementia.
- Analysis:** Cox proportional-hazards models across 6 nested adjustment sets; restricted cubic splines and interaction terms tested dose-response and effect modification by sex, race/ethnicity, APOE-ε4, age, country of birth, and family history.

STUDY POPULATION

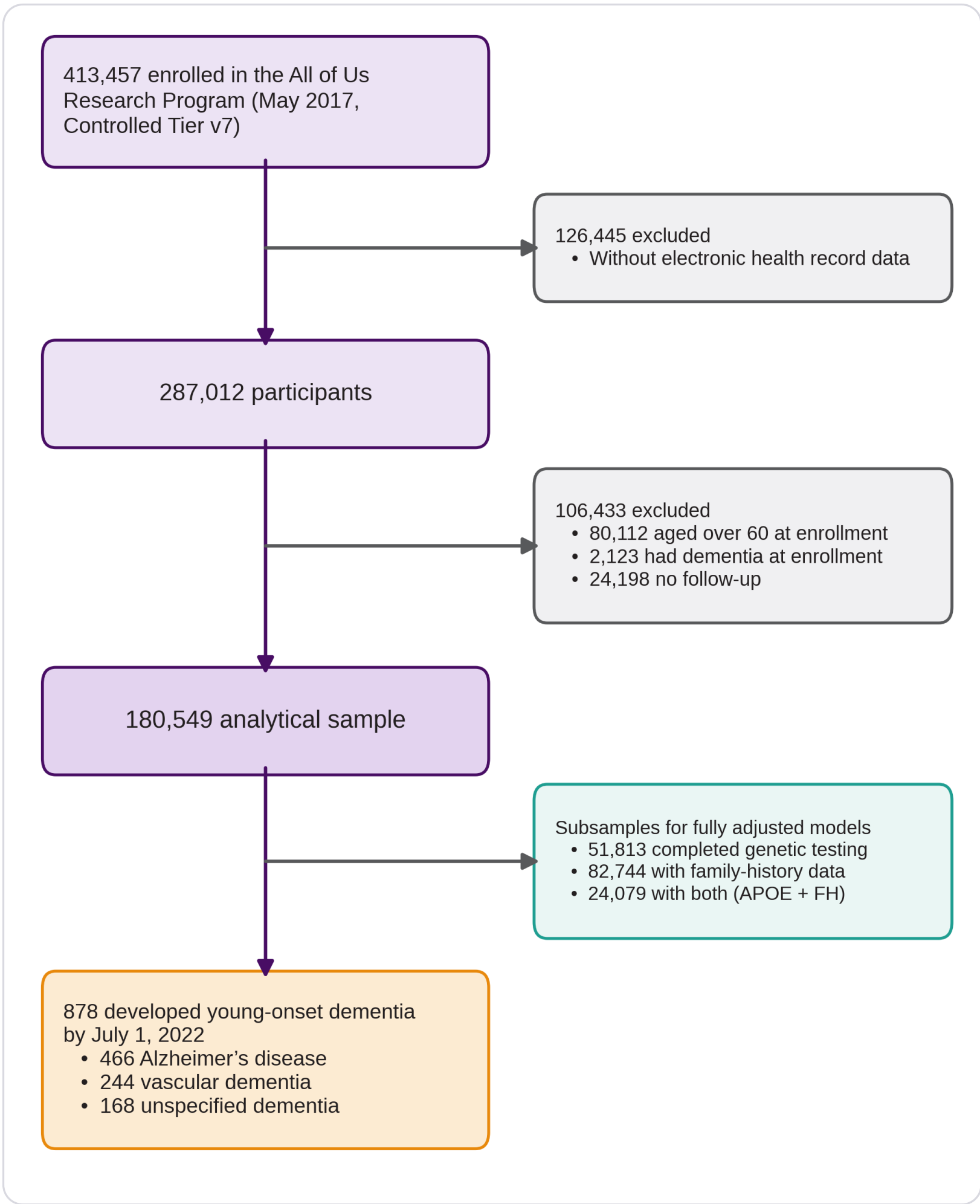


Figure 1. Sample selection. From 413,457 enrollees, 180,549 dementia-free adults under 60 were followed; 878 developed YOD

COHORT SNAPSHOT

Mean age: **53.8 years**
Sex: **52% female**
Mean follow-up: **33 months**
Genotyped (APOE-ε4): **51,813**
With family history of dementia: **82,744**



RESULTS

180,549
adults followed
(dementia-free, <60 yrs)

878
incident YOD cases

+44%
all-cause YOD risk
(Q5 vs Q1, adjusted)

1.94×
young-onset Alzheimer's
risk (Q5 vs Q1)

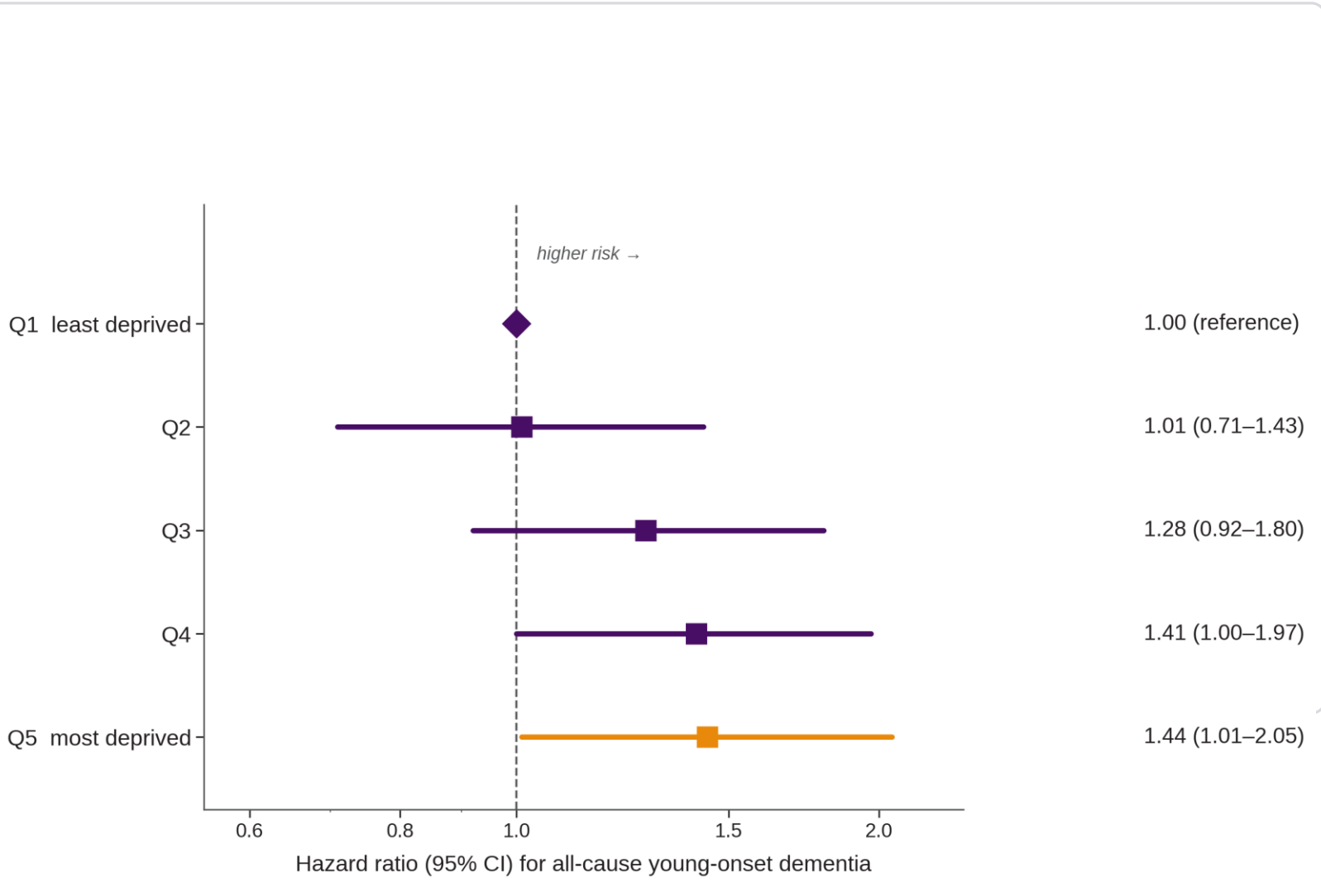


Figure 2. Fully adjusted hazard ratios for all-cause YOD rise stepwise across NDI quintiles (Q1 = reference). Q5 vs Q1 HR 1.44 (95% CI 1.01 to 2.05).

DOSE-RESPONSE

Each 1% higher NDI corresponded to about **2.6% higher all-cause YOD risk** and about **3.9% higher young-onset Alzheimer's risk**.

WHO IS MOST AFFECTED

Associations were stronger in **women and in non-Hispanic Black participants**, and were consistent across age, APOE-ε4 status, and family history.

RESULTS BY SUBTYPE

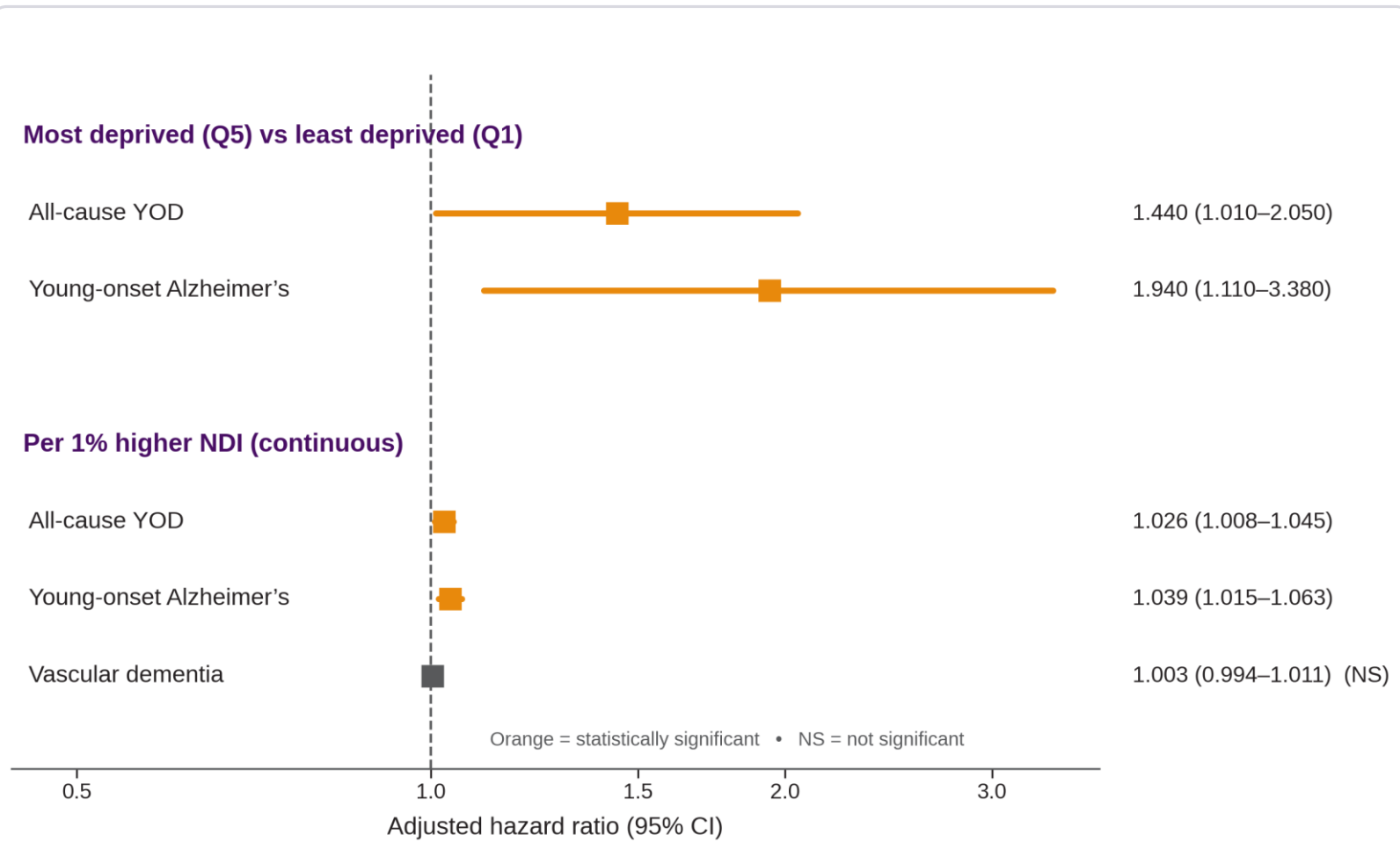


Figure 3. The association was strongest for young-onset Alzheimer's disease and was not statistically significant for vascular dementia after full adjustment.

CONCLUSIONS

Neighborhood deprivation is an important, **potentially modifiable risk factor** for YOD, independent of genetic risk.

Improving neighborhood conditions is a promising **upstream target for dementia prevention and health equity**.

Findings were consistent across six nested adjustment models and were independent of APOE-ε4 genotype and family history.

LIMITATIONS

Observational design limits causal inference. Mean follow-up was 33 months, and EHR-based ascertainment may underestimate incident young-onset dementia.

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