

The Adverse Social Exposome and Lewy Body Neuropathology: A Potential Pathway to Prevention

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BACKGROUND

Adverse social exposome: cumulative harmful exposure to social and environmental factors throughout the life-course

- Fundamentally modifiable
- Linked to Alzheimer’s disease (AD)

Lewy body dementia (LBD):

- In-vivo biomarkers not widely available
- Few known risk factors: older age, sex, family history

No studies have examined the interrelationship between the adverse social exposome and Lewy body neuropathology.

METHODS

Study Sample: Brain donors from two sites (n=1,182; donations: 1985-2018).

Adverse Social Exposome Determination:

- Fully characterized donor residential histories
- Time-concordant values of **Area Deprivation Index (ADI)**
- Sensitive periods: Early (ages 0-18), Mid (ages 19-64), Late (ages 65+); Last known residential address
- Cumulative Exposure:** number of years living in high ADI (above sample median)
- Higher Exposure:** high donor median ADI (sample 75-percentile)

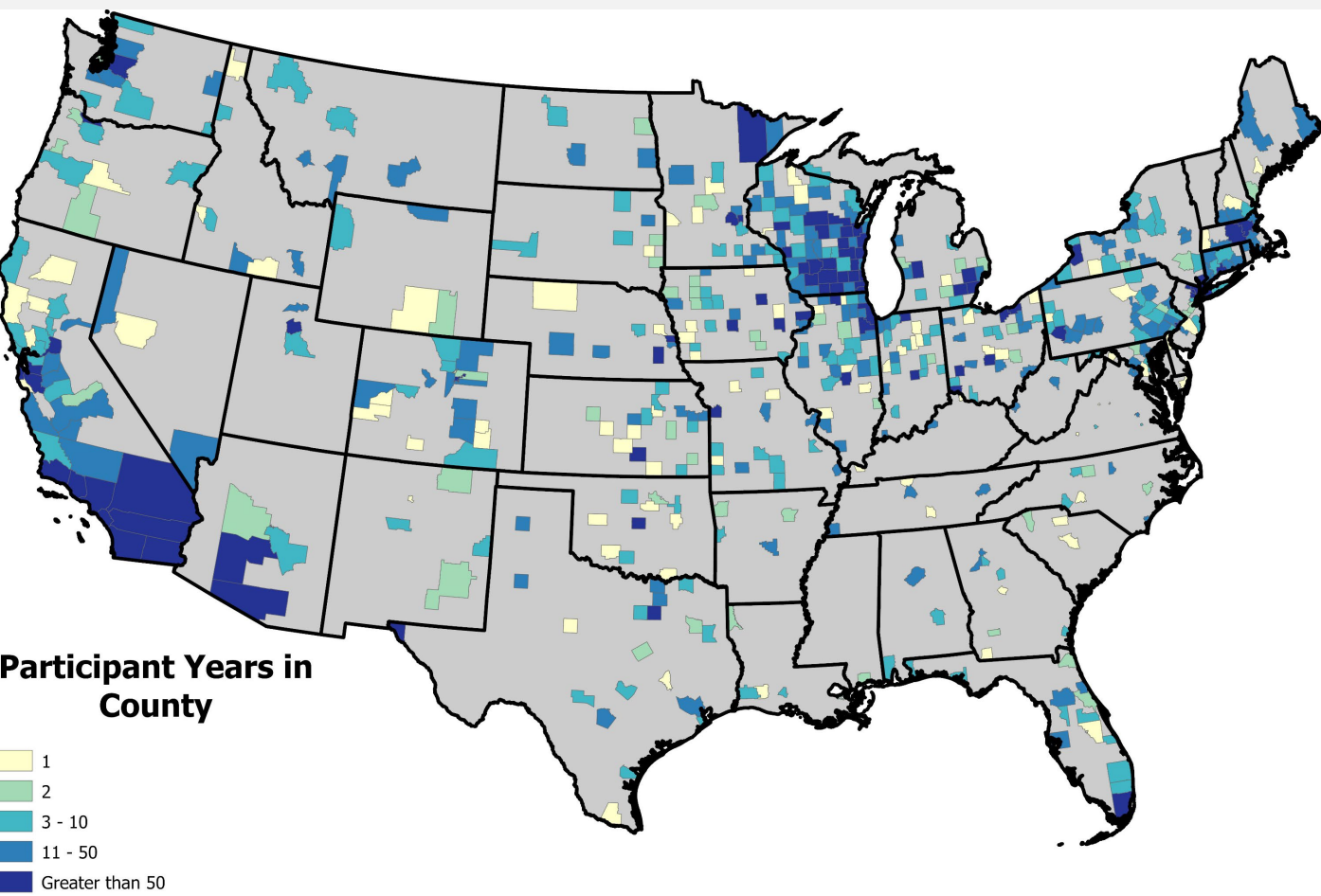
Outcome: Presence of Lewy body neuropathology

Covariates: Age, sex, and highest level of education

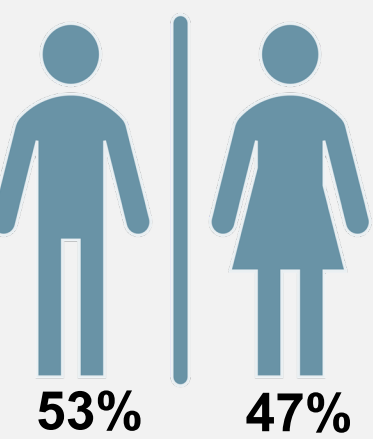
Statistical analyses: multiple imputation chain equations; pooled multivariate logistic regression models

SAMPLE CHARACTERISTCS

Map of Lifetime Donor Residential Histories



Sex



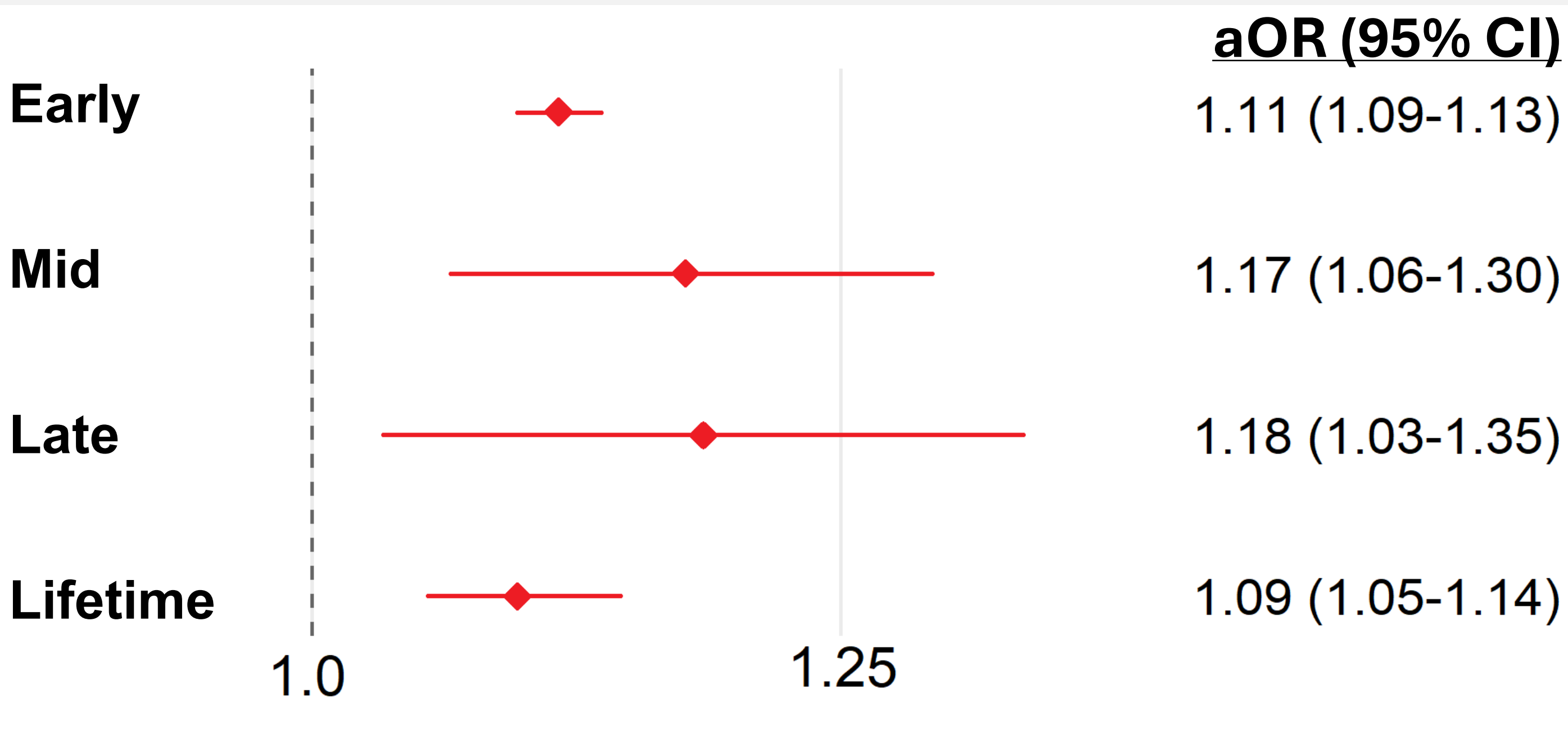
Race

88% White

Life-course data spanning 1900-2017

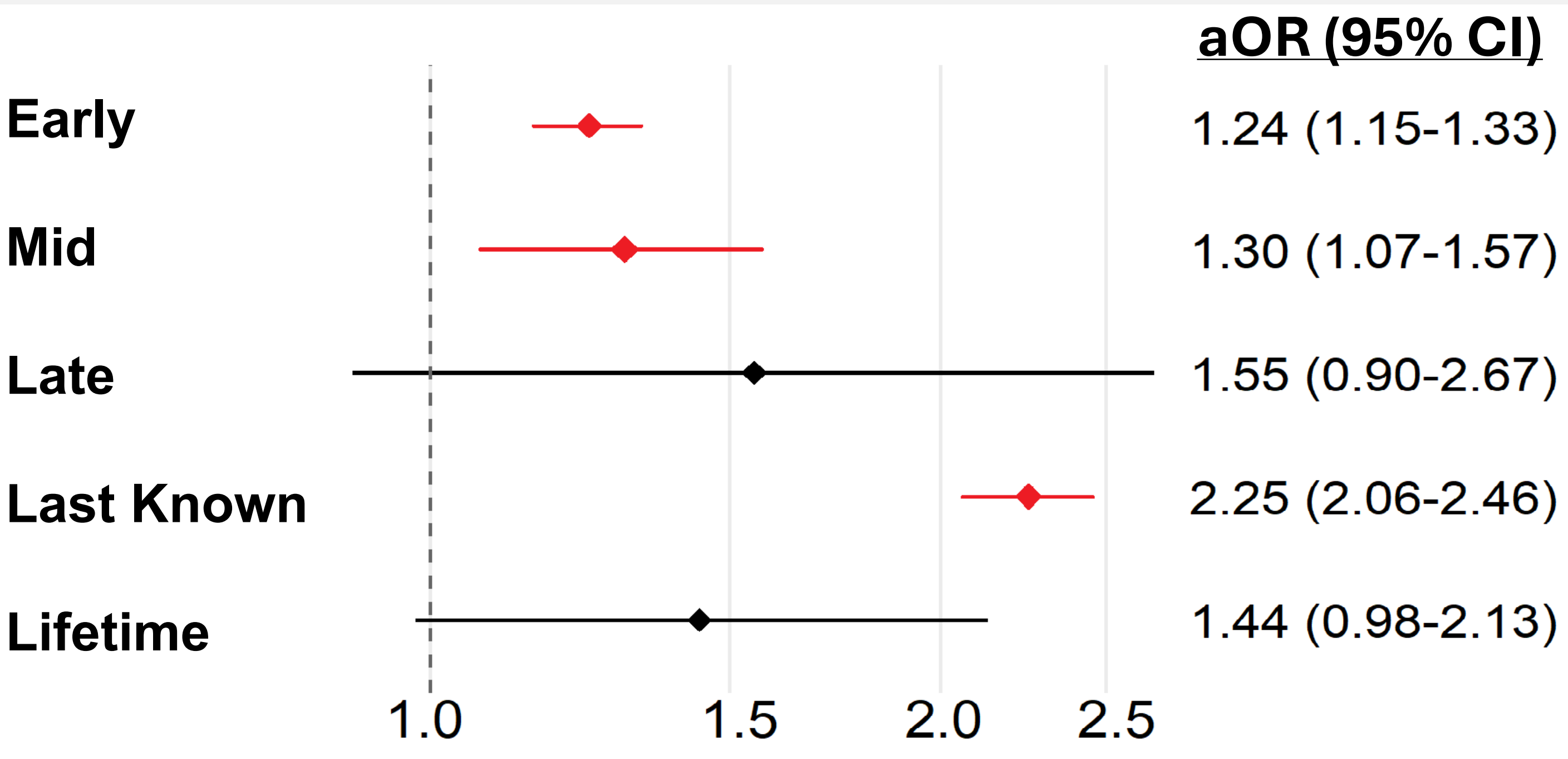
RESULTS

Cumulative Exposure in Sensitive Periods



Cumulative exposure to the adverse social exposome increased odds of Lewy body neuropathology throughout the life-course. Every **5 additional years** living in high ADI adverse social exposomes in mid and late life was linked to **17-18%** increased odds of Lewy body neuropathology.

Higher Exposure in Sensitive Periods



Living in a higher ADI adverse social exposome in early and midlife increased the odds of Lewy body neuropathology by over **20%** compared to donors living in lower ADI exposomes. At last known residence, higher ADI was linked to **more than a two-fold increase** in odds of Lewy body neuropathology.

DISCUSSION

High ADI adverse social exposomes linked to greater odds of Lewy body neuropathology, with associations persisting throughout the life-course

- Midlife as important exposure window hinting at potential underlying biological mechanisms
- Strongly suggests the adverse social exposome and related toxic social and environmental exposures, contribute to Lewy body neuropathology risk

Limitations: Predominantly White/non-Hispanic, highly educated sample living in lower ADI areas compared to the United States population

Impact: Leveraging the **modifiable** adverse social exposome with future blood-based biomarker discoveries to **revolutionize risk reduction and prevention in LBD.**

Next Steps: Replicate study in a larger and more diverse brain bank and further characterize staging and clinical correlates of LBD neuropathology.

CONCLUSIONS

The adverse social exposome via high ADI is linked to Lewy body neuropathology providing **tremendous opportunity to reduce or mitigate risk** for Lewy body neuropathology earlier in the life-course.

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