

Associations Of 20-year Trajectories Of Systemic Inflammation With Structural Brain Imaging Markers And Incident Dementia In Aging Adults



Stroke, Cognition, and
Neuroepidemiology Lab

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BACKGROUND

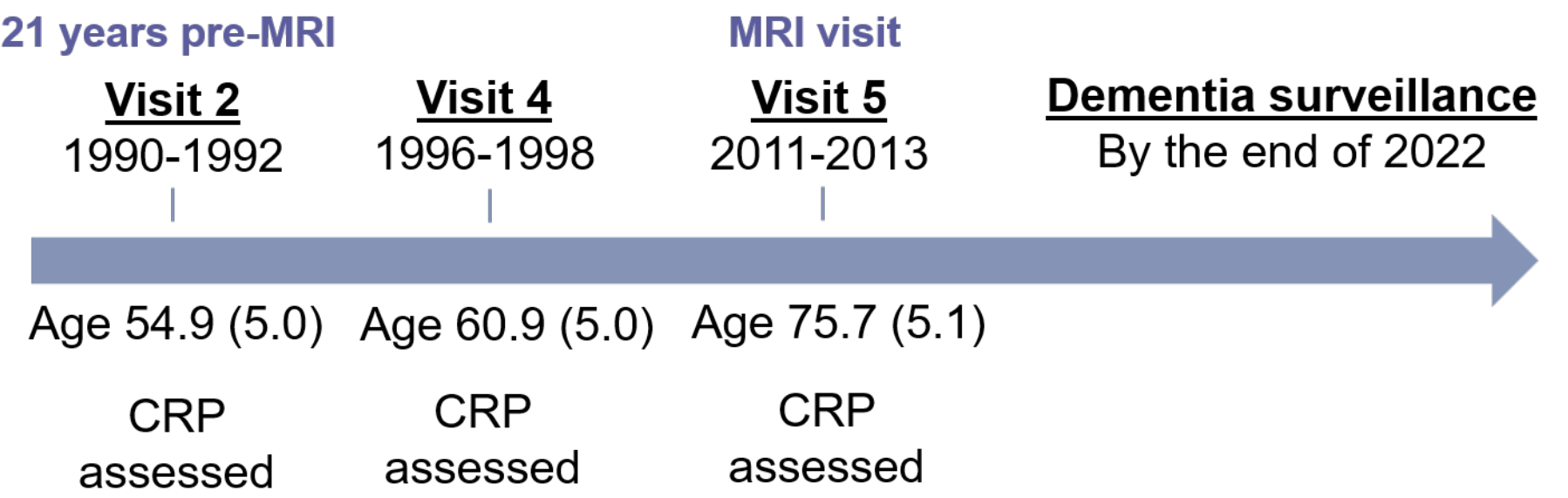
- Systemic inflammation** has been implicated in dementia risk and adverse brain structural outcomes.
- Whether and how **longitudinal inflammatory patterns** from midlife into late life affect **brain health** in later life remains unclear.

Objectives:

- Examine associations between **systemic inflammation trajectories and dementia incidence, white matter hyperintensity (WMH) lesion volume, and hippocampal volume**.
- Test whether **associations vary by age** at the start of the trajectory.

METHODS

- 3,879 middle-aged and older adults** in the Atherosclerosis Risk in Communities (ARIC) study
- Dementia-free and attended an in-person visit in late life (Visit 5)
- Exposure: C-reactive protein (CRP) trajectories** derived from Visits 2, 4, and 5 over 20+ years using latent class mixed models
- Outcomes: Incident dementia** (follow-up up to 11 years through 2022), **WMH and hippocampal volumes** (MRI subsample, n=1,201)
- Statistical analyses:** Cox proportional hazards models, linear regression, with trajectory-by-age group interactions, and mediation analysis
- Covariates:** Progressive adjustment for demographic, vascular risk, and clinically related characteristics



Participant Characteristics (Visit 2)

Age group, n (%)	
<50 years	623 (16.1)
50-54 years	1,391 (35.9)
55-59 years	1,080 (27.8)
≥60 years	785 (20.2)
Female, n (%)	2,206 (56.9)
Black race, n (%)	662 (17.1)
>high school, n (%)	1,758 (45.3)

RESULTS

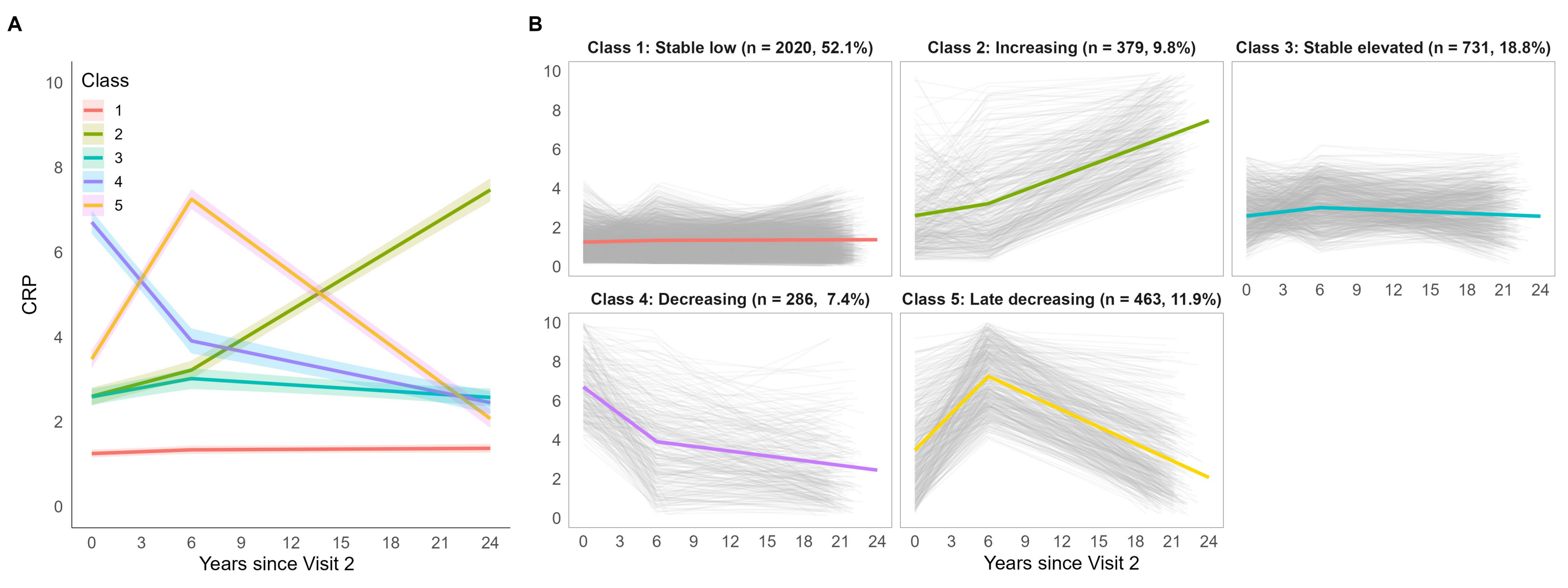


Figure 1. CRP trajectories from Visit 2 to Visit 5, 1990-2013 (A) Mean predicted trajectory patterns over time (years) with shaded areas representing 95% CIs. (B) Individual participant CRP trajectories (thin gray). The mean trajectory for each class is overlaid in bold color.

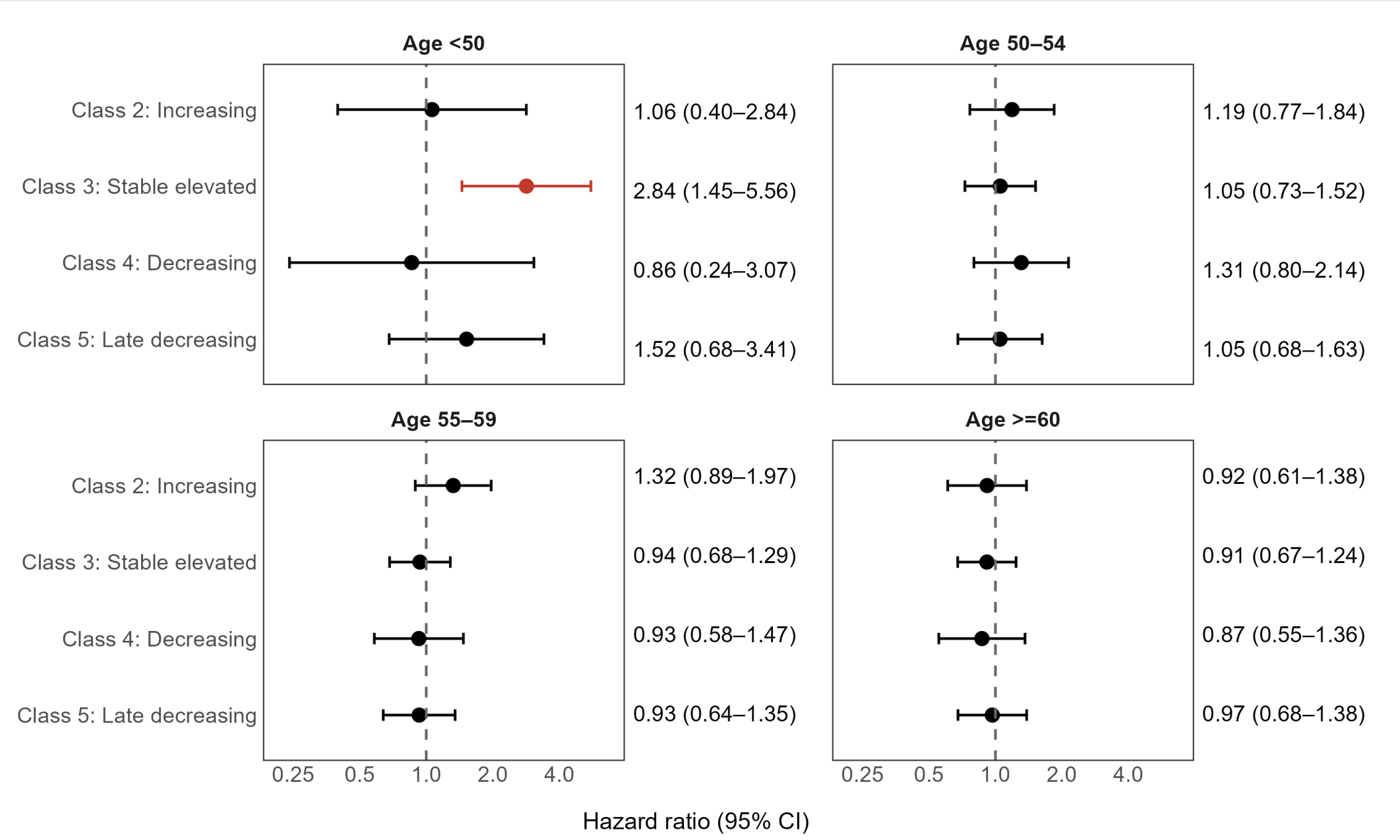


Figure 2. Age-stratified hazard ratios for incident dementia associated with CRP trajectories (vs stable-low) Hazard ratios and 95% confidence intervals for **incident dementia** comparing each CRP trajectory with stable-low trajectory were estimated from age-stratified Cox models. Overall CRP trajectory-by-age group interaction: $p=0.370$.

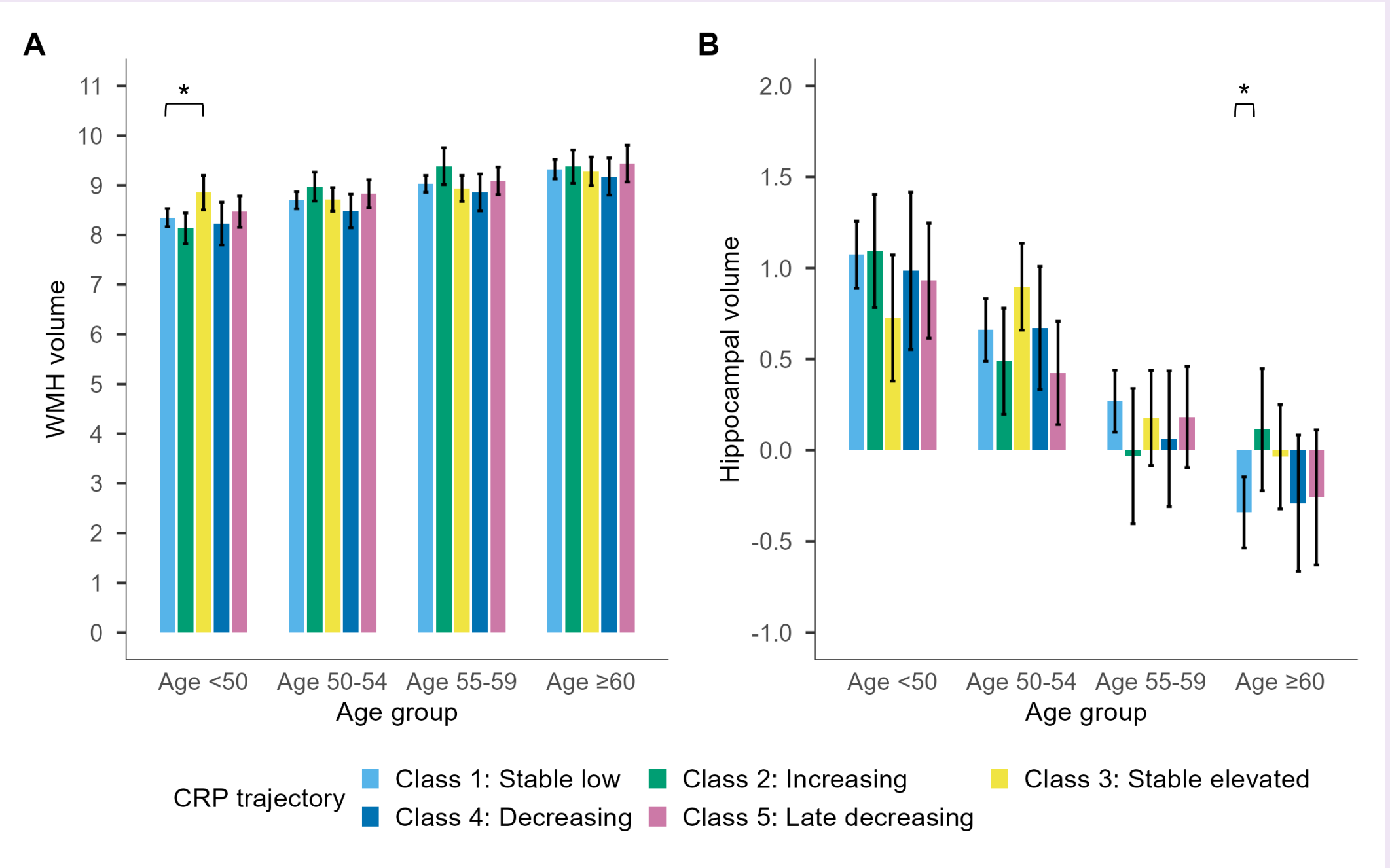


Figure 3. Age-specific associations between CRP trajectories and structural brain imaging markers in the MRI subsample Bars show estimated marginal predicted means for (A) **total WMH volume** and (B) **hippocampal volume**, derived from linear regression models weighted for selection into the MRI subsample. Overall CRP trajectory-by-age group interaction: total WMH volume $p=0.070$; hippocampal volume $p=0.014$.

RESULTS

- No overall associations** between CRP trajectories and:
 - Dementia risk
 - WMH volume
 - Hippocampal volume
- Age-specific associations:**
 - Adults <50y** at the start of the trajectory:
 - Stable-elevated (vs stable-low) trajectory associated with higher dementia risk
 - Stable-elevated trajectory associated with greater WMH volume
 - Adults aged 60+** at the start of the trajectory:
 - Increasing (vs stable-low) trajectory associated with relatively preserved hippocampal volume
- Mediation:**
 - Neither** WMH nor hippocampal volume **mediated** CRP trajectory-dementia association

CONCLUSIONS

- Persistent systemic inflammation from midlife** associated with **adverse brain outcomes** – only among adults <50y at the start of the trajectory.
- Age-specific associations** suggest an age-related shift in the inflammatory risk profile.
- Longitudinal CRP trajectories** from midlife through late life capture age-specific associations with brain health.
- Alternative pathways** linking early midlife inflammation to dementia warrant further investigation.

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CONTACT



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