

Artificial Intelligence–derived Vascular Age from Photoplethysmography is Associated with Brain Structural Alterations across Major Brain Networks

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✓ TAKE-HOME MESSAGE

Higher PPG-derived vascular age gap is associated with widespread brain structural alterations, particularly in memory and executive networks, supporting its potential as a scalable digital biomarker of vascular brain aging.

14,593

MRI participants

5

Brain networks

32%

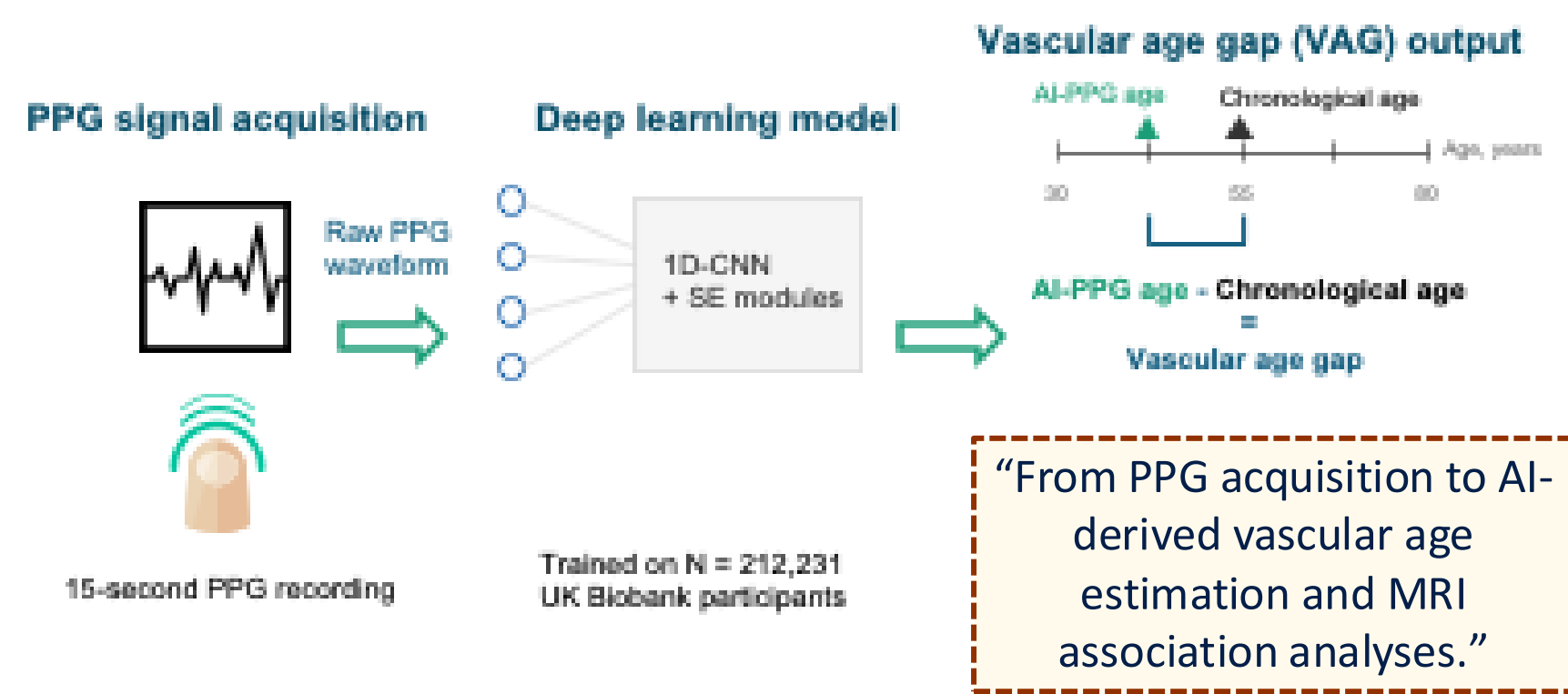
Higher dementia risk

BACKGROUND & OBJECTIVE

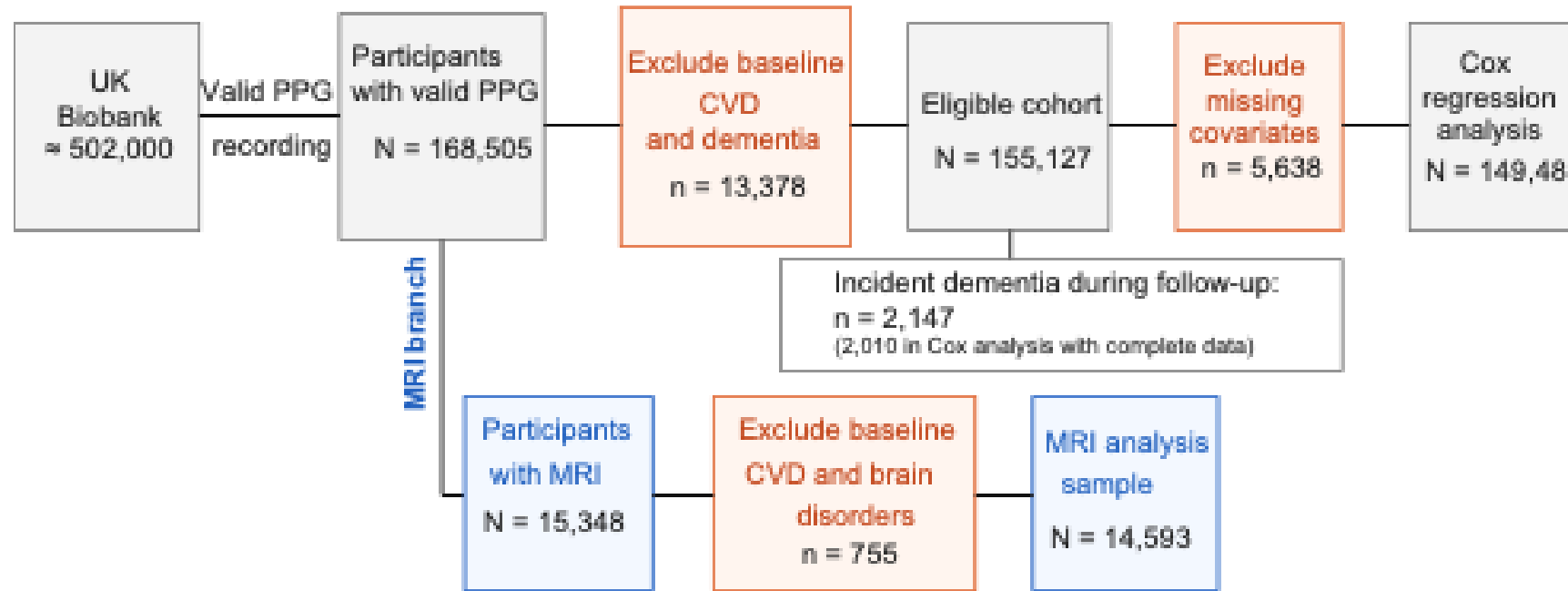
- **Vascular aging** contributes to **dementia**, but conventional **cardiovascular risk factors** incompletely capture vascular health.
- **Deep learning** can estimate vascular age from **photoplethysmography (PPG)**, a non-invasive and scalable signal.
- **Objective**: determine whether **vascular age gap (VAG)** is associated with **multimodal MRI markers** across major brain networks.

STUDY DESIGN & ANALYSIS

Step 1. AI-derived vascular age estimation

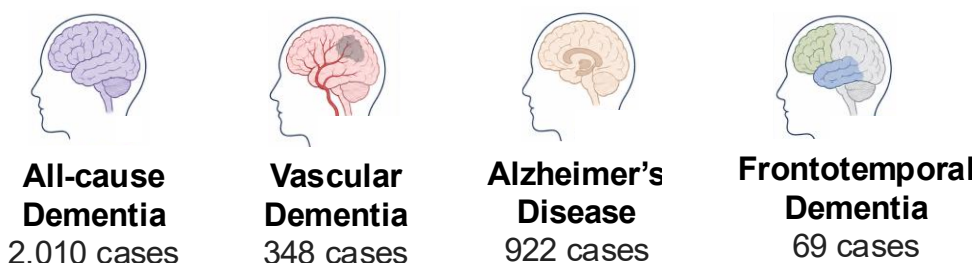


Step 2. Participant selection



Step 3. Statistical analysis

Dementia Outcomes



Analytic Framework

Primary association
 - Cox proportional hazards models
 - Vascular age gap as continuous and categorical exposure

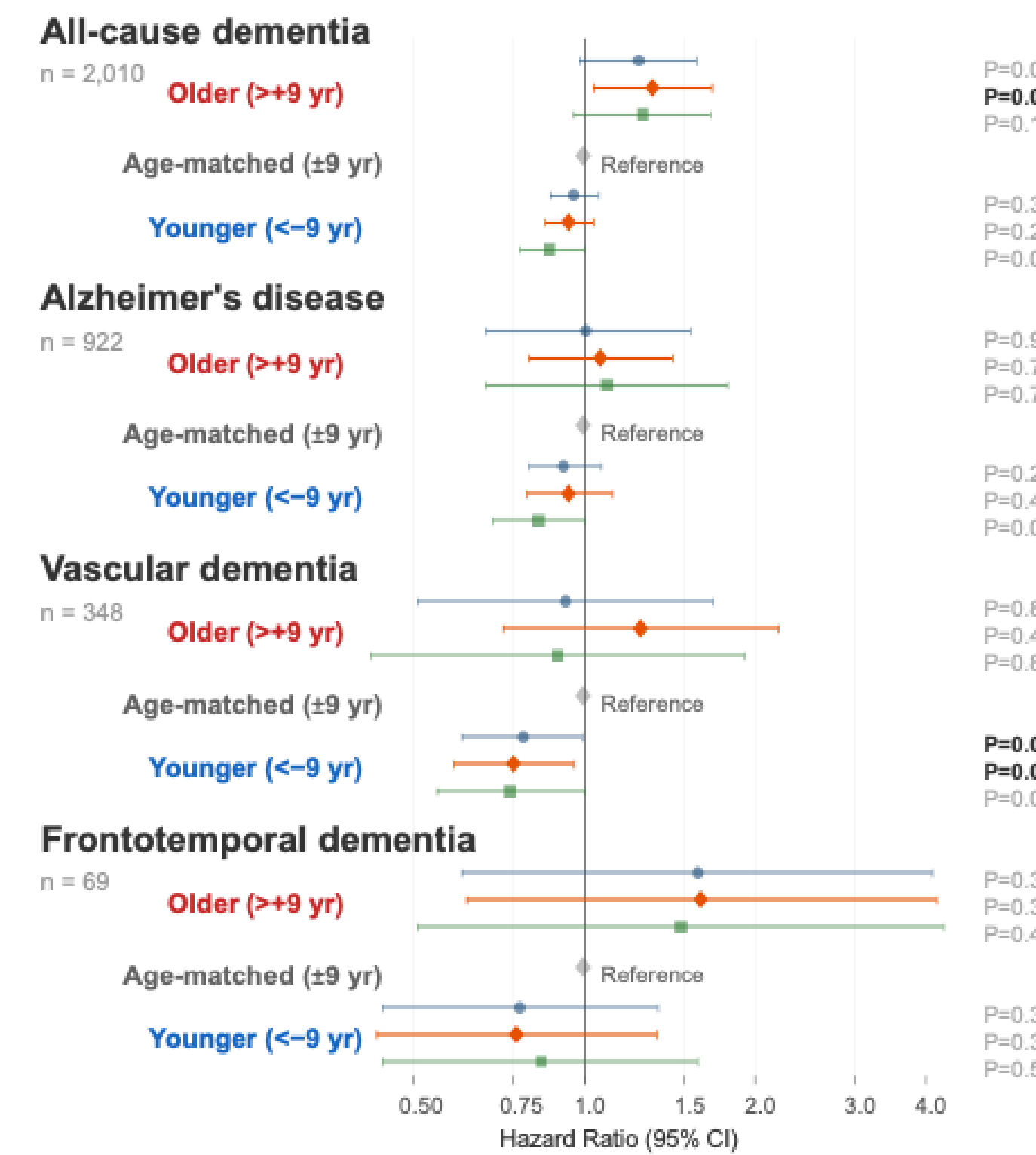
Competing-risk analysis
 - Fine–Gray subdistribution hazard models
 - Death as competing event
Non-linear dose–response
 - Restricted cubic splines

Adjustment Strategy

Primary model adjusted for demographics, APOE ε4, lifestyle and baseline cardiovascular risk factors.

“The AI-derived vascular age gap (VAG) was subsequently evaluated in the MRI subcohort using multivariable regression analyses.”

RESULT 1 · ASSOCIATIONS BETWEEN VASCULAR AGE GAP AND INCIDENT DEMENTIA



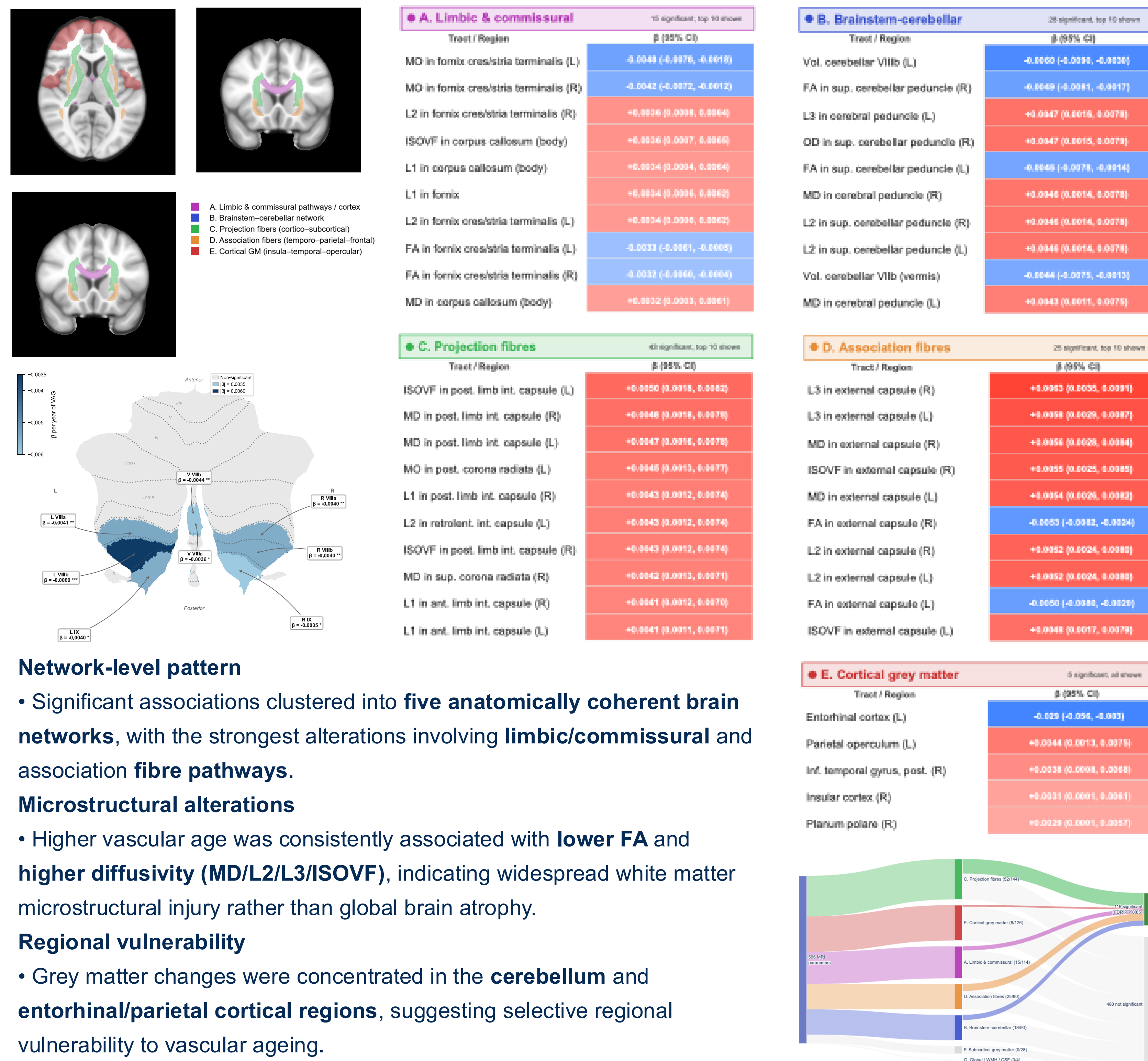
Main Results

- Participants with **vascular age >9 years** older than their chronological age had a **32% higher risk of incident all-cause dementia** after adjustment for baseline and follow-up cardiovascular risk factors (HR 1.32, 95% CI 1.04–1.68).
- **Younger vascular age (<9 years)** was associated with a **25% lower risk of vascular dementia** (HR 0.75, 95% CI 0.59–0.96).

Interpretation

- Associations remained **robust after adjustment for follow-up cardiovascular risk factors** and in participants who remained free of incident cardiovascular disease, suggesting that vascular age provides information beyond conventional cardiovascular risk.

RESULT 2 · DISTINCT BRAIN NETWORKS ASSOCIATED WITH VASCULAR AGE GAP



Network-level pattern

- Significant associations clustered into **five anatomically coherent brain networks**, with the strongest alterations involving **limbic/commissural** and **association fibre pathways**.
- Higher vascular age was consistently associated with **lower FA** and **higher diffusivity (MD/L2/L3/ISOVF)**, indicating widespread white matter microstructural injury rather than global brain atrophy.
- Grey matter changes were concentrated in the **cerebellum** and **entorhinal/parietal cortical regions**, suggesting selective regional vulnerability to vascular ageing.

RESULTS AT A GLANCE

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MRI phenotypes associated

Cerebellum + Entorhinal cortex
 Selective grey-matter loss

Robust

Independent of CVRFs & incident CVD

FA↓ / MD↑

Predominant white-matter injury

Most affected brain regions

Memory & executive

- Fornix
- External capsule
- Entorhinal cortex
- Parietal operculum

Brainstem–cerebellar

- Superior cerebellar peduncle
- Cerebellum VIIIb
- Internal capsule

BIOLOGICAL INTERPRETATION

Distributed brain ageing

- PPG-derived vascular age reflects distributed rather than focal brain structural alterations.

White matter vulnerability

- White matter microstructure appears more sensitive to vascular ageing than global brain volume.

Dementia-relevant pathways

- The strongest alterations involve limbic and association pathways supporting memory and executive function.

Beyond traditional risk

- Associations persist after adjustment for conventional cardiovascular risk factors.

CONCLUSION

Main conclusion

- AI-derived vascular age identifies early structural brain ageing beyond conventional cardiovascular risk assessment.

Clinical implication

- A 15-second wearable PPG recording may enable scalable screening of vascular brain health.

Future direction

- Prospective validation using longitudinal wearable PPG is warranted.

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KEY FINDINGS

- ✓ Higher vascular age was linked to **widespread white matter** injury across multiple brain networks.
- ✓ Greater vascular age was associated with **selective cerebellar and cortical grey matter loss**.
- ✓ Older vascular age (>9 years) predicted a **32% higher risk of incident dementia**.
- ✓ Associations were **independent of conventional cardiovascular risk factors** and remained robust in sensitivity analyses.