



Dementia-related modifiable risk factor exposure accelerates brain ageing and lower cognitive performance in healthy adults

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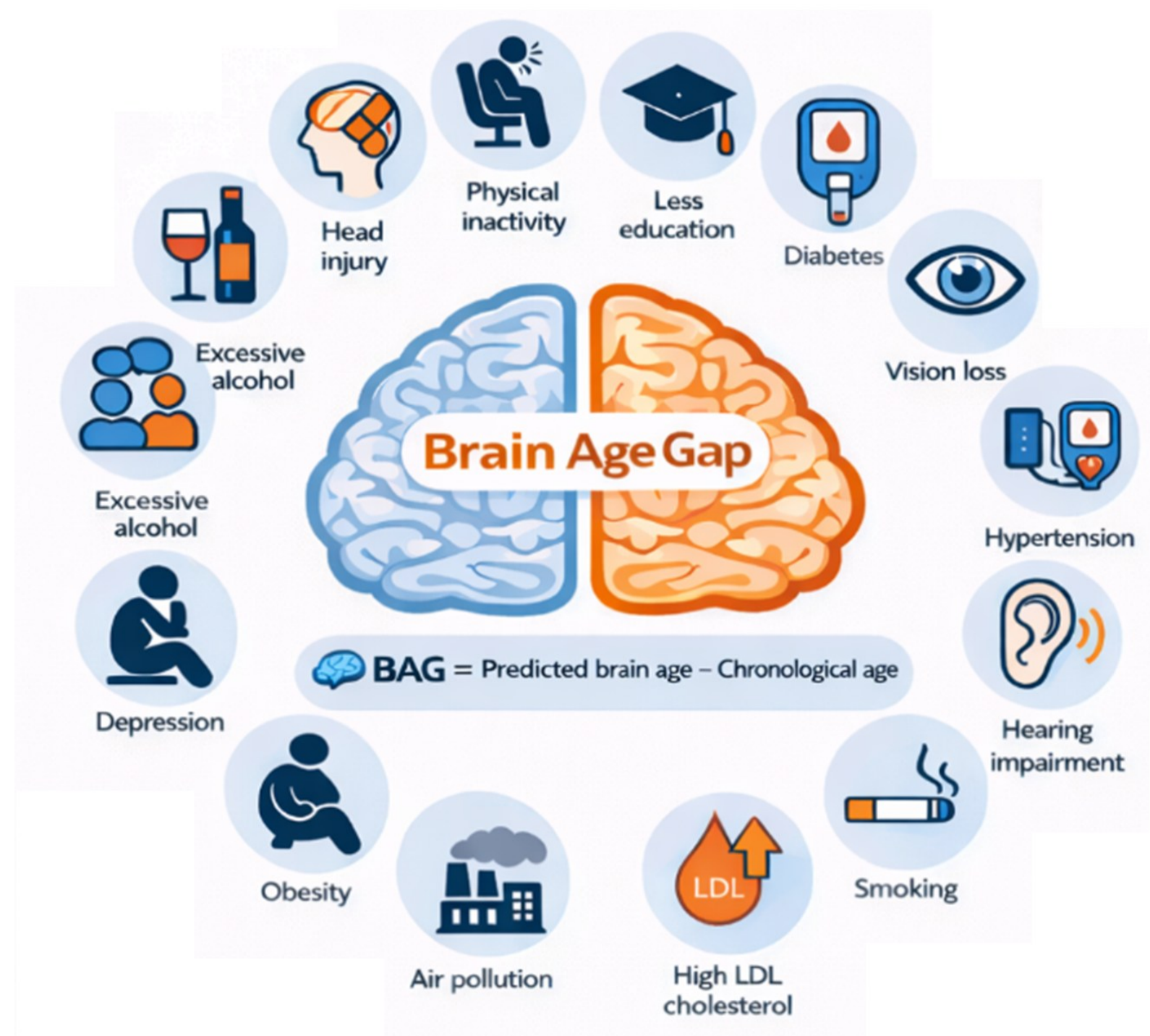
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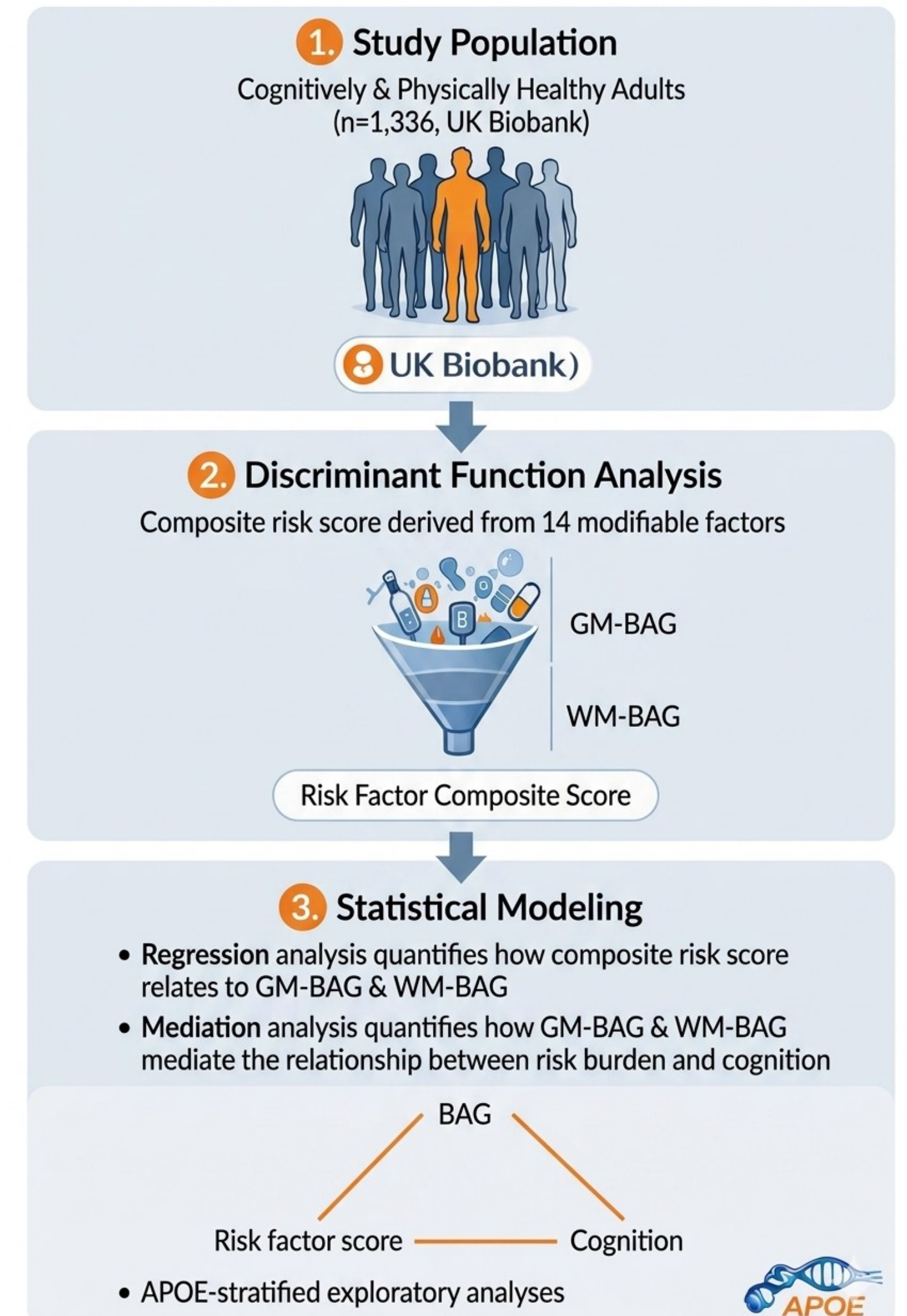
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Introduction

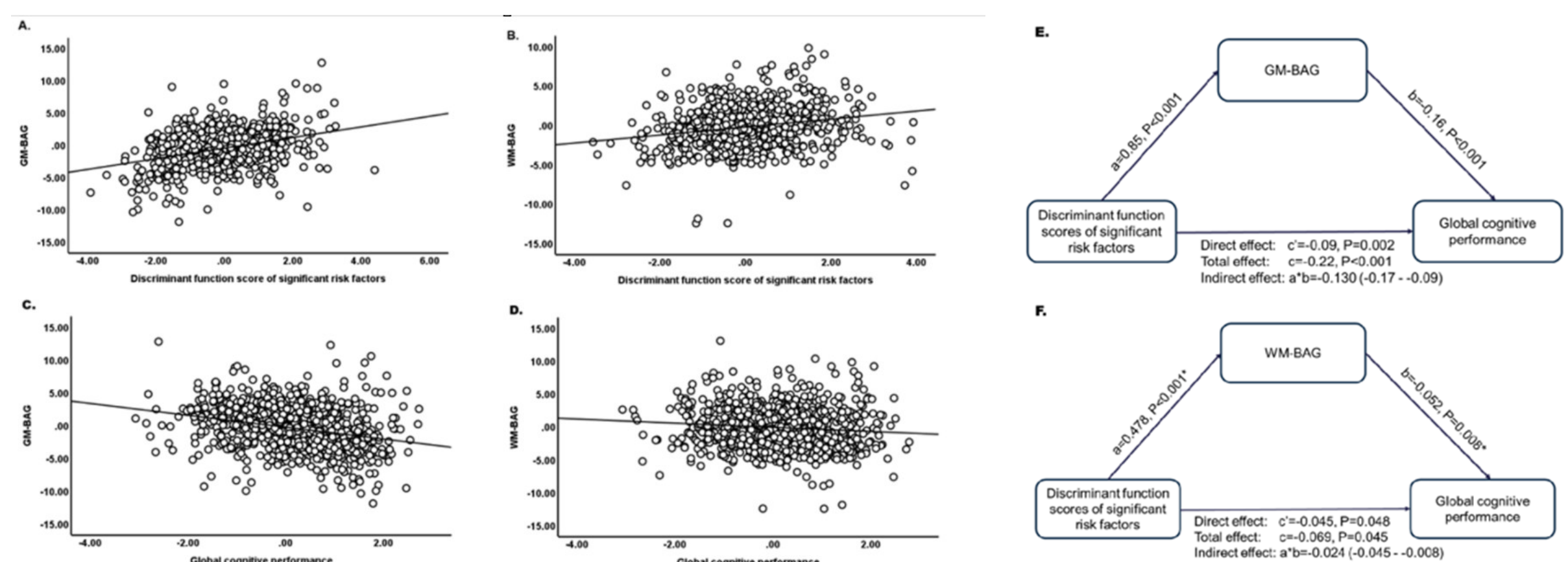
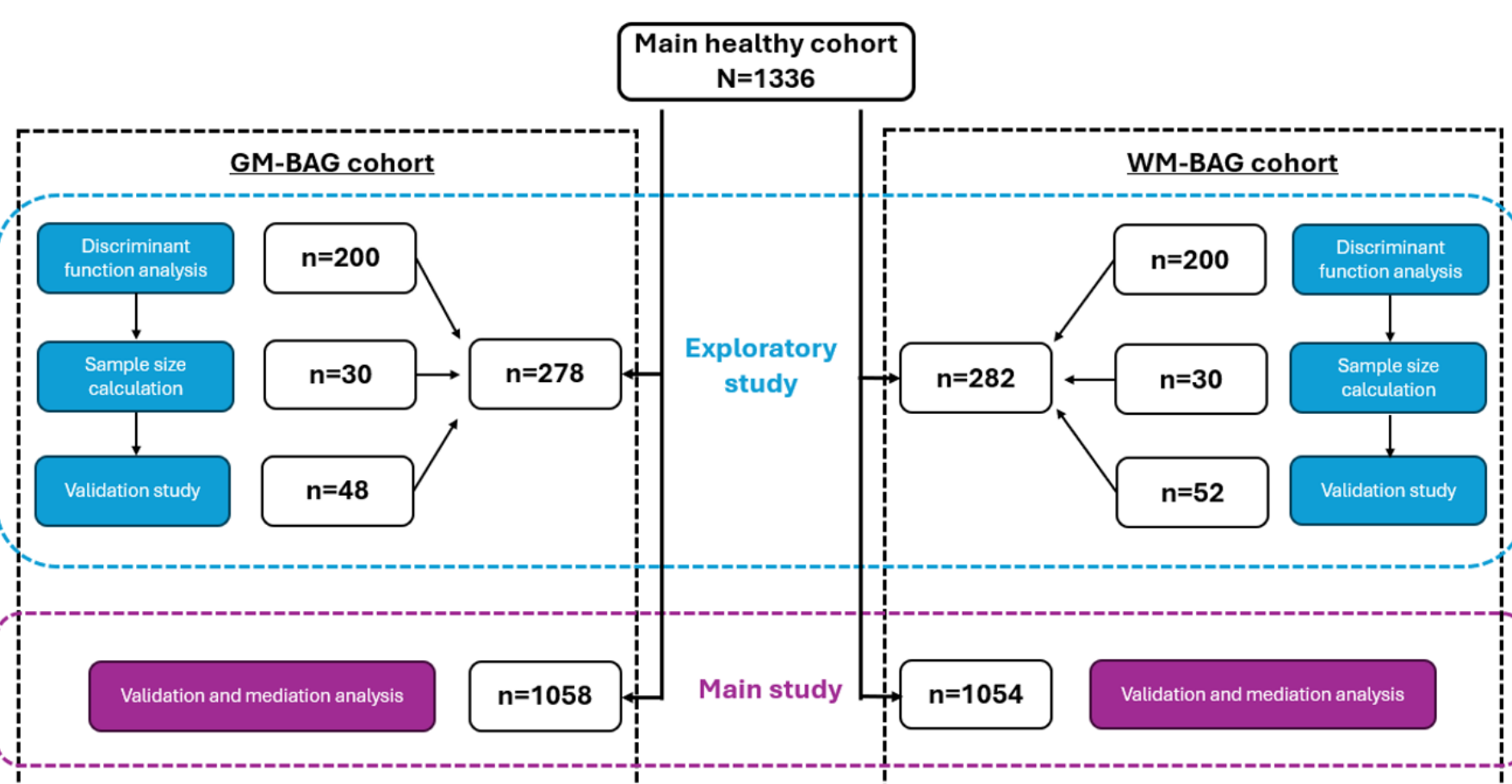


1. How modifiable risks drive early brain changes remains unclear.
2. BAG is an MRI-based biomarker reflecting cumulative lifetime exposure.
3. Tissue-specific BAG links risk burden to accelerated brain ageing and cognition.

Methods



Results



1. 5 key modifiable factors differentiated high vs. low GM- and WM- BAG.

GM-BAG: Lower education, higher systolic BP, smoking, air pollution, **hearing impairment**

WM-BAG: Lower education, higher systolic BP, smoking, air pollution, **higher BMI**

2. Higher cumulative risk burden was associated with older-appearing GM- and WM-BAG.

3. Tissue-specific BAG partially mediated the association between modifiable risk burden and cognition.

4. Mediation effect is strongest in the neutral/intermediate APOE genotypes.

Conclusions

1. Modifiable midlife risk factors were associated with accelerated tissue-specific brain ageing which in turn related to global cognitive performance.
2. Our findings offer mechanistic insight into how modifiable risk factors drive brain ageing in cognitively and physically healthy people.