

# What best predicts cognitive change?

## Disentangling multimodal predictors of cognitive reserve and trajectory in ageing

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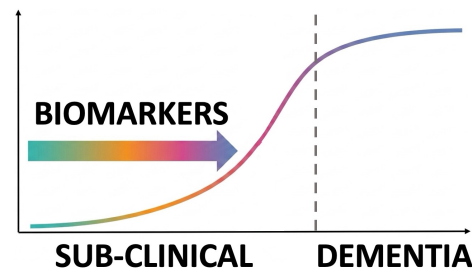
### INTRODUCTION



We usually diagnose cognitive problems only after functional impairment appears



But post-clinical treatments have limited ability to stop or reverse decline in later life



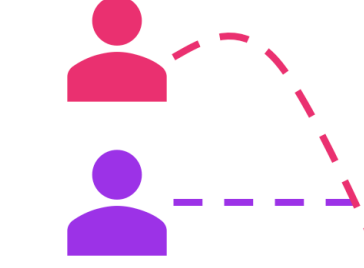
Multiple screening modalities can detect risk decades before cognitive symptoms emerge



But population-scale cognitive health screening requires both accuracy and efficiency



**Question 1:** Which screening measures best predict cognitive change across domains?



**Question 2:** Can we predict not only where someone is, but where they're going?

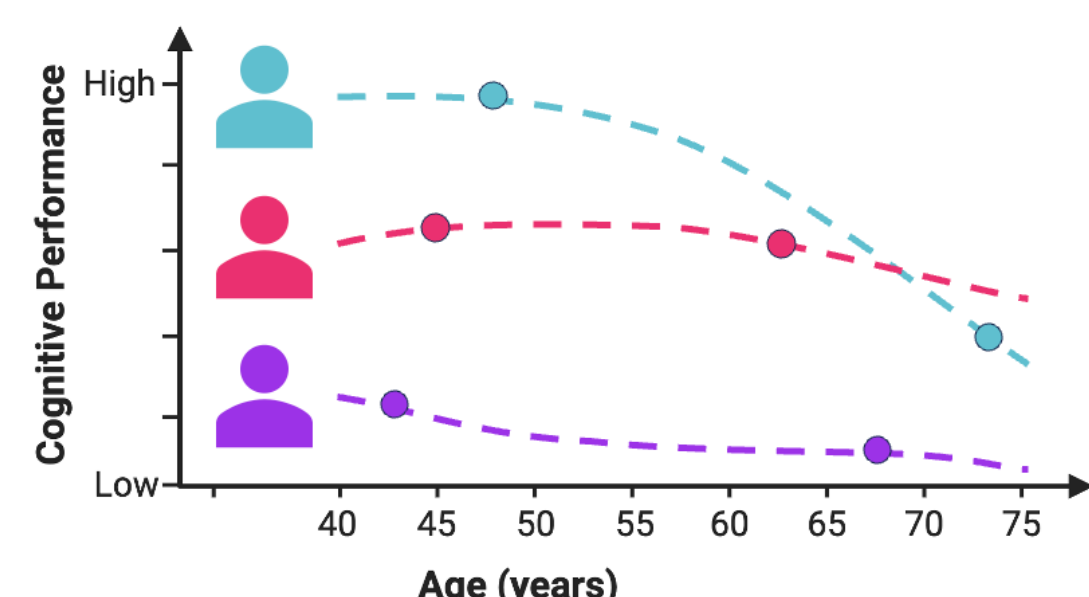


**Aim:** Establish data-driven recommendations for baseline screening measures that best predict cognitive reserve and cognitive trajectory

### METHODS



$n = 8,170$  participants from the UK biobank with longitudinally repeated cognitive assessments

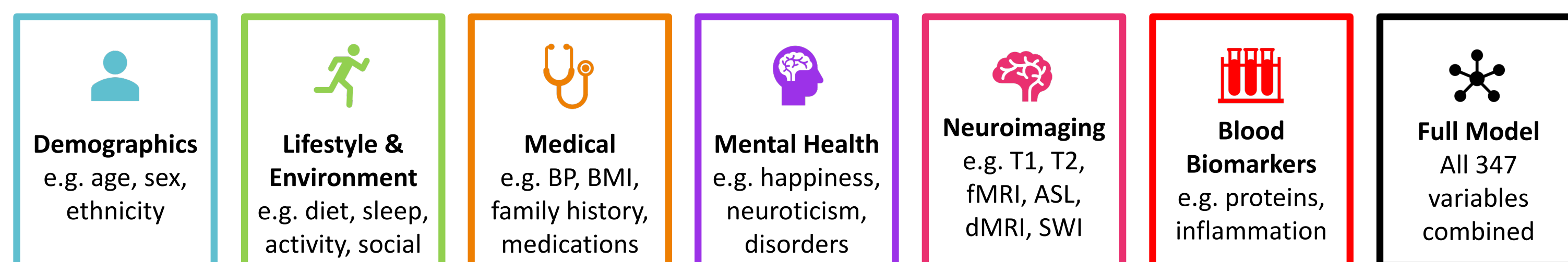


Trail Making Task | Symbol Digit Test | Pairs Memory Test | Fluid Intelligence Test | Reaction Time: Snap

#### Bifactor Exploratory Structural Equation Model

Latent Cognitive Domains

347 Baseline Screening Variables



#### Random Forest Prediction

56 separate models  
7 modality categories x 4 cognitive domains x 2 timepoints

#### Multilevel Modelling

$$\text{Cognition}_{(ij)} = \beta_0 + \beta_1(\text{Mean}_i) + \beta_2(\text{Deviation}_{(ij)}) + u_{0i} + \epsilon_{(ij)}$$

#### Cognitive Reserve

Inter-individual differences  
Mean performance across repeated assessments

#### Cognitive Trajectory

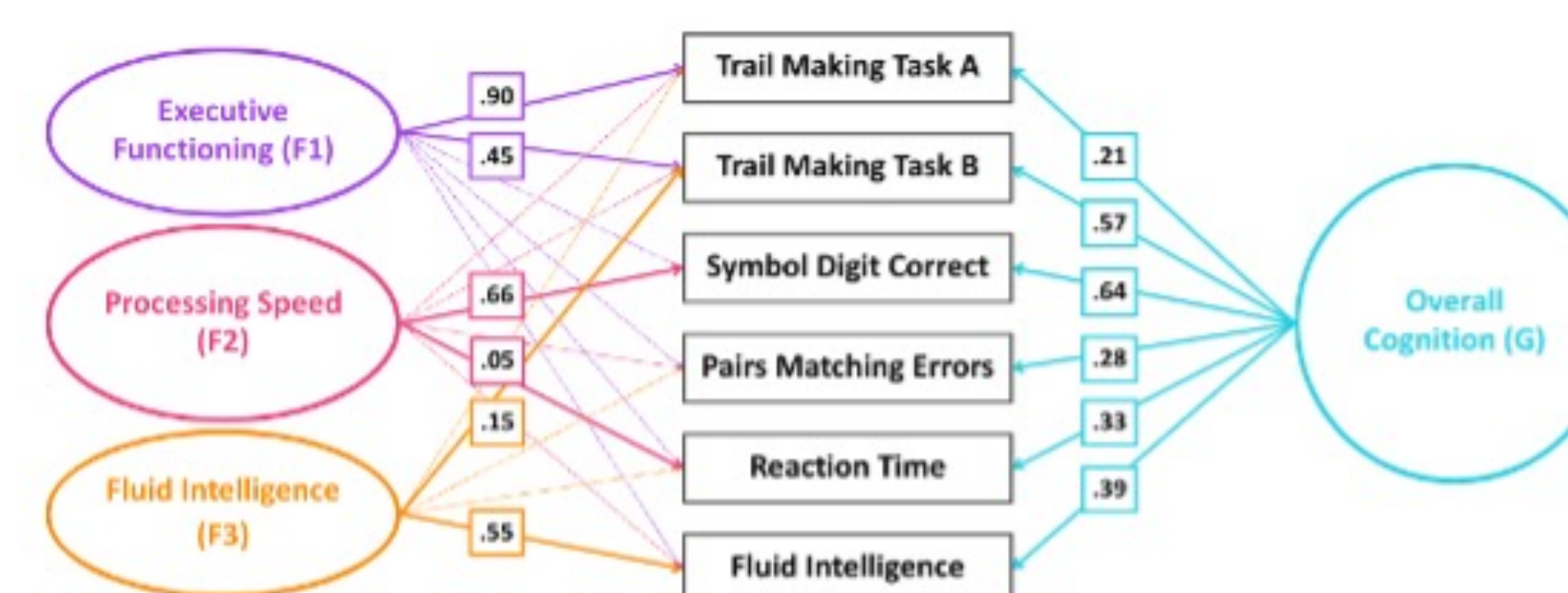
Intra-individual differences  
Deviations from an individual's mean over time

#### Commonality Analysis

How much of each model's predictive performance reflects cognitive reserve versus cognitive trajectory?

### RESULTS

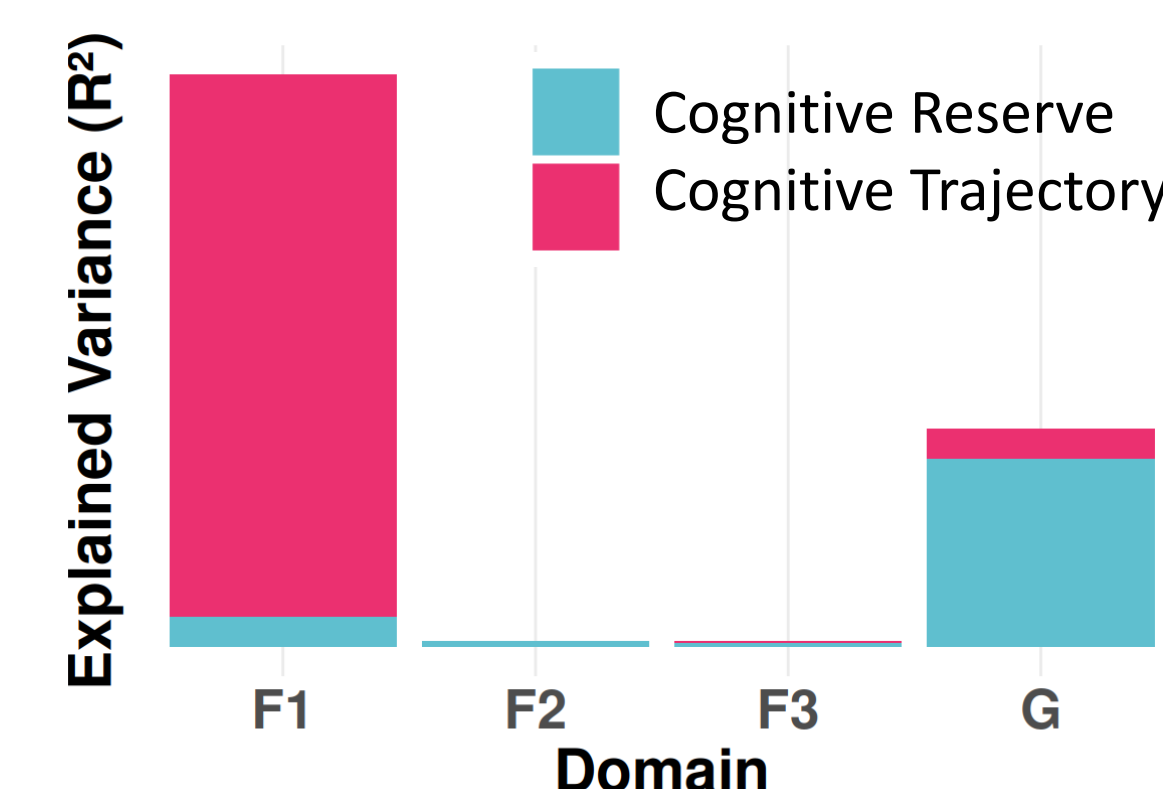
#### Bifactor Exploratory Structural Equation Model



5-fold CV EFA → ESEM  
yielded four cognitive factors (F1, F2, F3, G)

G-factor explained 49% of all cognitive variance

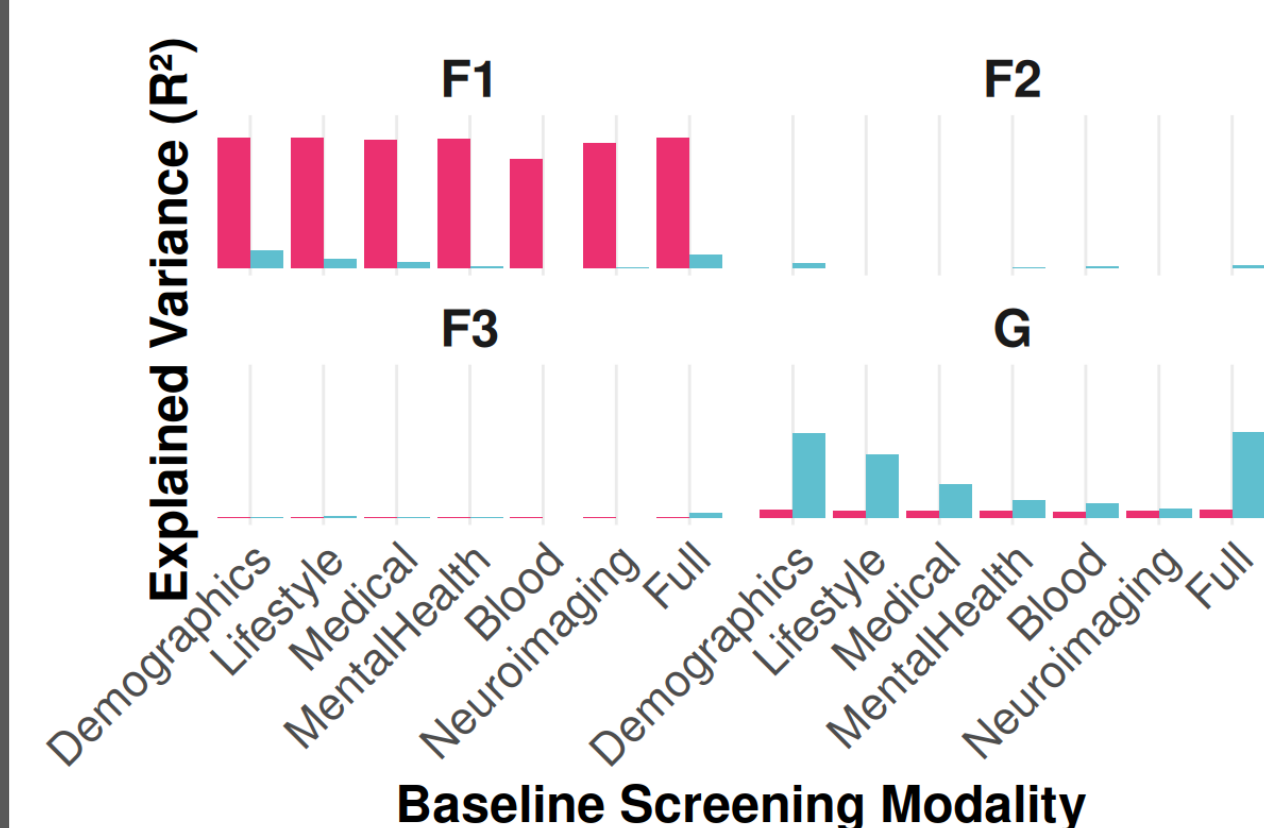
#### Multilevel Modelling & Commonality Analyses



Predictability varied markedly by cognitive domain

#### Executive function (F1)

22–31% total variance explained  
91% of prediction reflects future change  
46% of within-person variance explained



#### Overall Cognition (G)

3–19% total variance explained  
92% of prediction reflects cognitive reserve  
only 10% within-person variance explained

Demographics, Environment, and Lifestyle explained most prediction of overall cognition

#### Marginal Permutation Importance

Within a category of predictors what matters most?



Most screening modalities identified the same key predictors regardless of cognitive domain



However, neuroimaging showed more domain-specific predictive patterns

### TAKE-HOME MESSAGE

#### Screen Efficiently

Prioritise demographic, lifestyle, and environmental screening for efficient cognitive health prediction

#### Predict Trajectory

Focus prediction on executive function to best capture future cognitive trajectory

#### Image Specifically

Explore neuroimaging when there is need for domain specific rather than broad predictive value

### Limitations & Future Directions

- Incorporate emerging biomarkers unavailable in UK Biobank
- Validate findings in representative clinical cohorts
- Extend modelling to earlier life and additional follow-up timepoints
- Translate prediction into targeted prevention and intervention
- Evaluate feasibility of population-scale cognitive health screening

### Acknowledgements

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Come say hello! I'd love to meet

