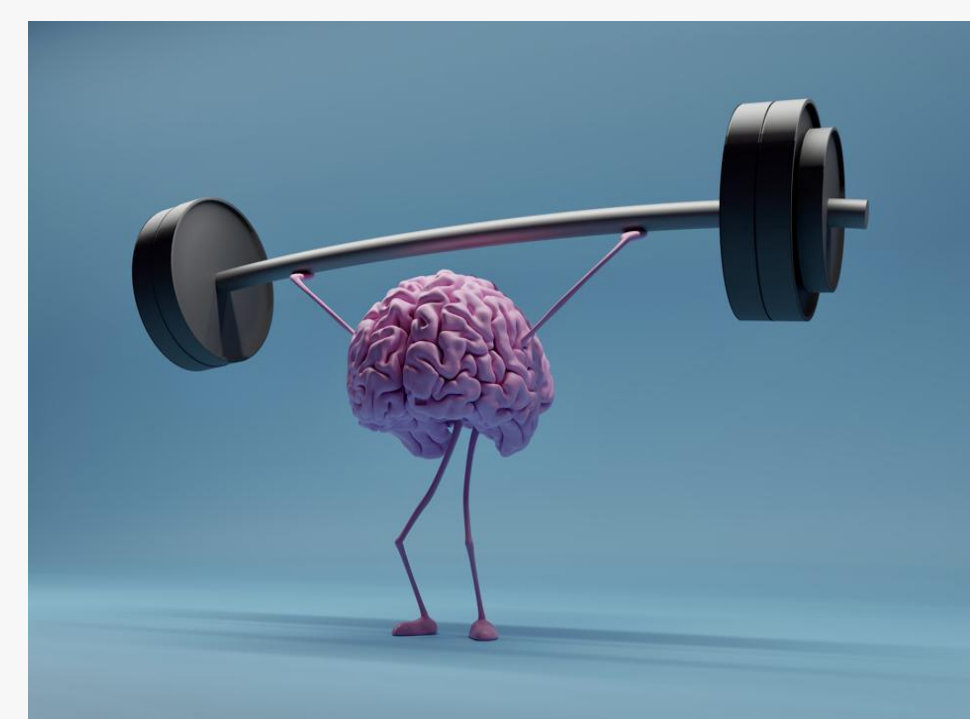


## Bioenergetics and Vascular Predictors of Potential Super-Ager and Cognitive Decline Trajectories – A UK Biobank study

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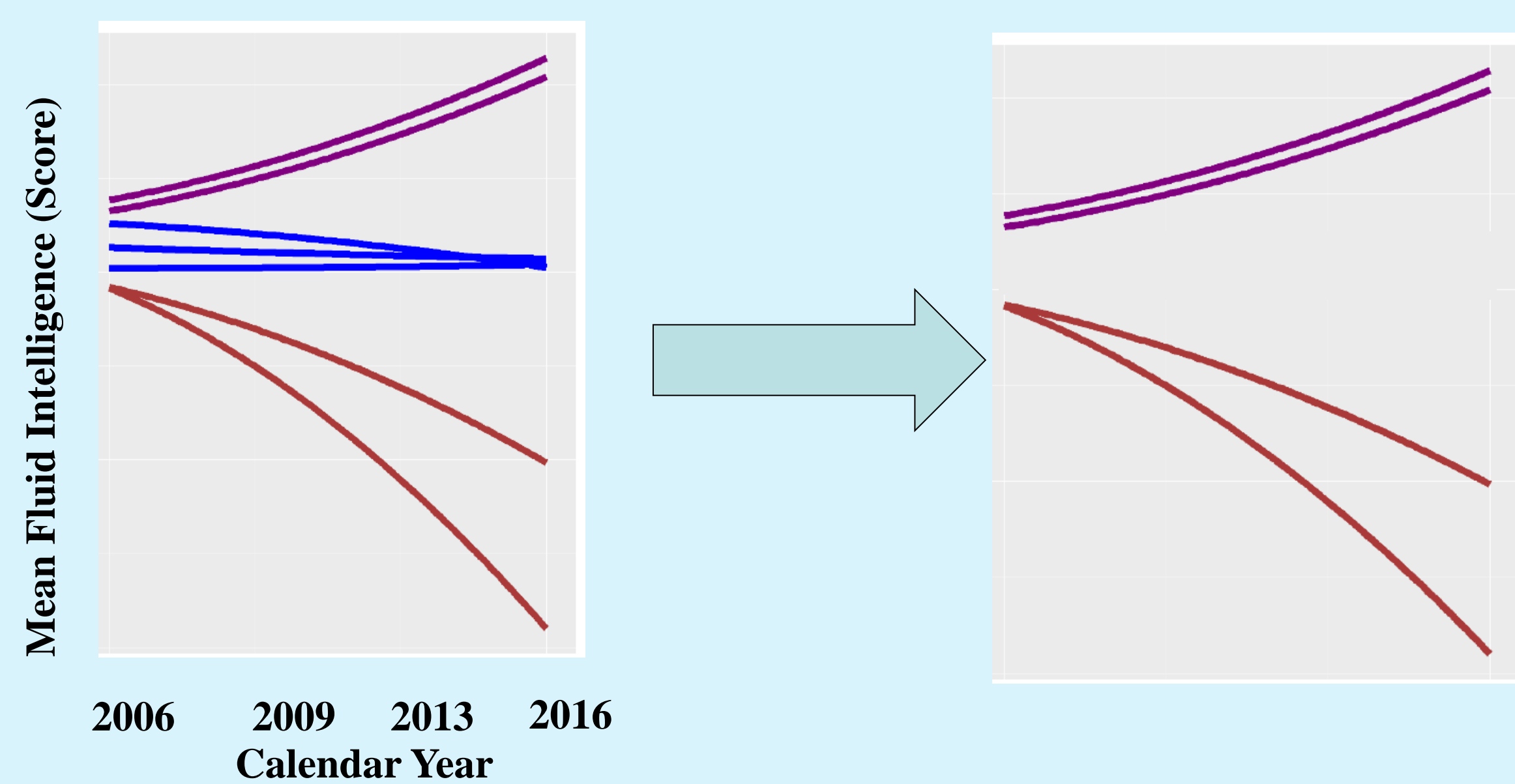
### Introduction

- **Ageing** has often been characterized by progressive decline in cognitive process, particularly executive function.
- **Super-Agers** characterized as adults aged 80 years or older, who have cognitive function similar to young adults.
- **Fluid intelligence (FI)** is a type of executive function defined as the capacity to solve the problems requiring logic without prior knowledge or experience. It indicated more degeneration than other cognitive domains in the aging.
- **Cognitive aging** is accompanied by changes in **vascular**, **bioenergetics**, and **immune** factors. How **biological** factors can explain or predict long-term gain vs. decline in cognitive function?
- **Current study** examined over 7-9 years a comprehensive set of biomarkers in middle-aged adults to distinguish between two groups that clearly showed either cognitive gain or decline using Random Forest (RF) classification model.



### Research Methods

- To define **Cognitive Trajectory Types**, for each the participant, FI's linear changes over time was calculated. These rate of changes in FI scores have been used to label the participants as **Positive-Ager**, **Cognitive Maintainer**, or **Cognitive Decliner**.

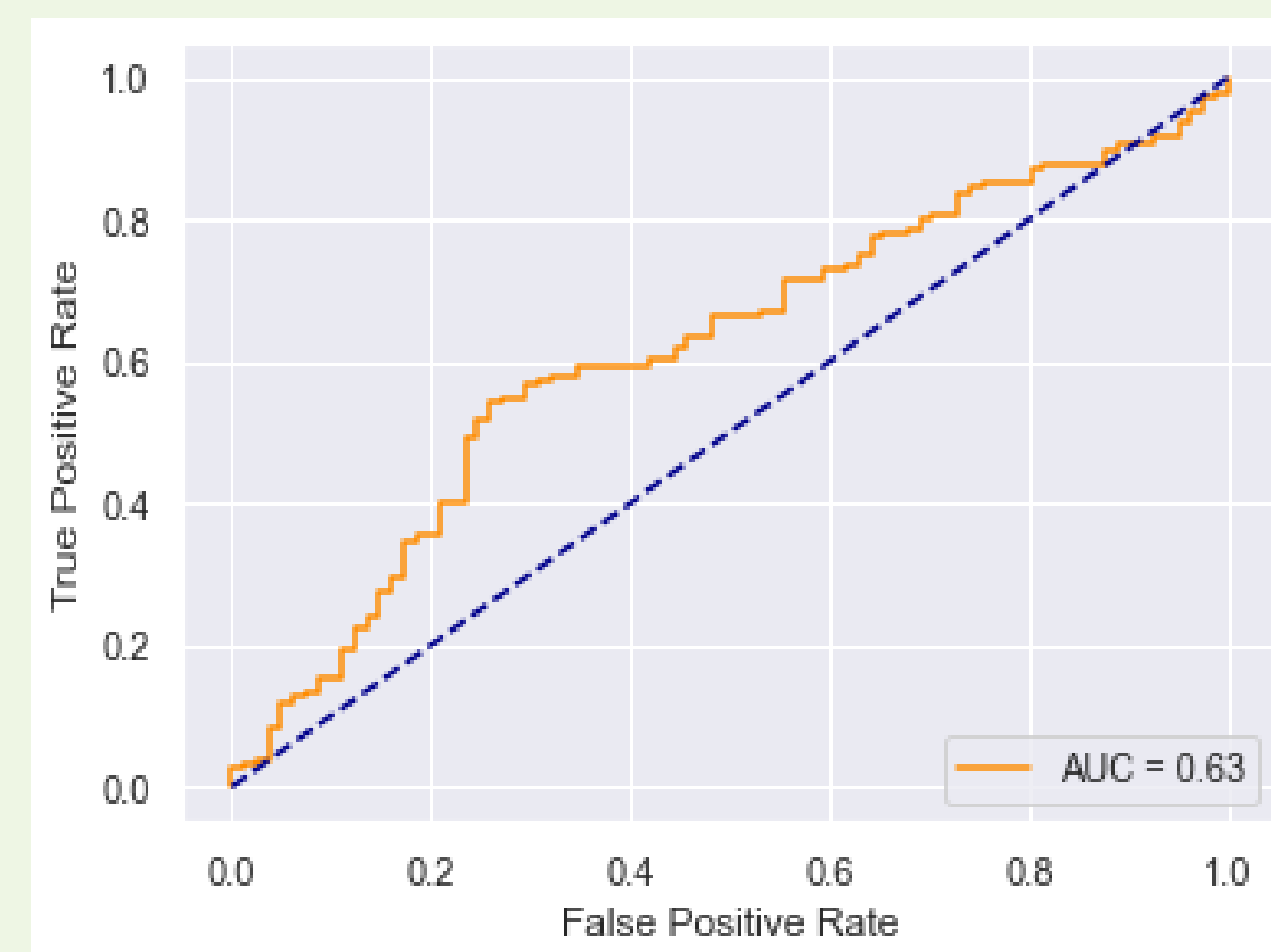


- **183** biological features, and covariates including age, sex, social class, education, and tobacco smoking were considered for the 943 participants.

- A RF Classification model have been tuned using Bayesian optimization to specify the hyper-parameters, then it trained and tested by training and test set, respectively.

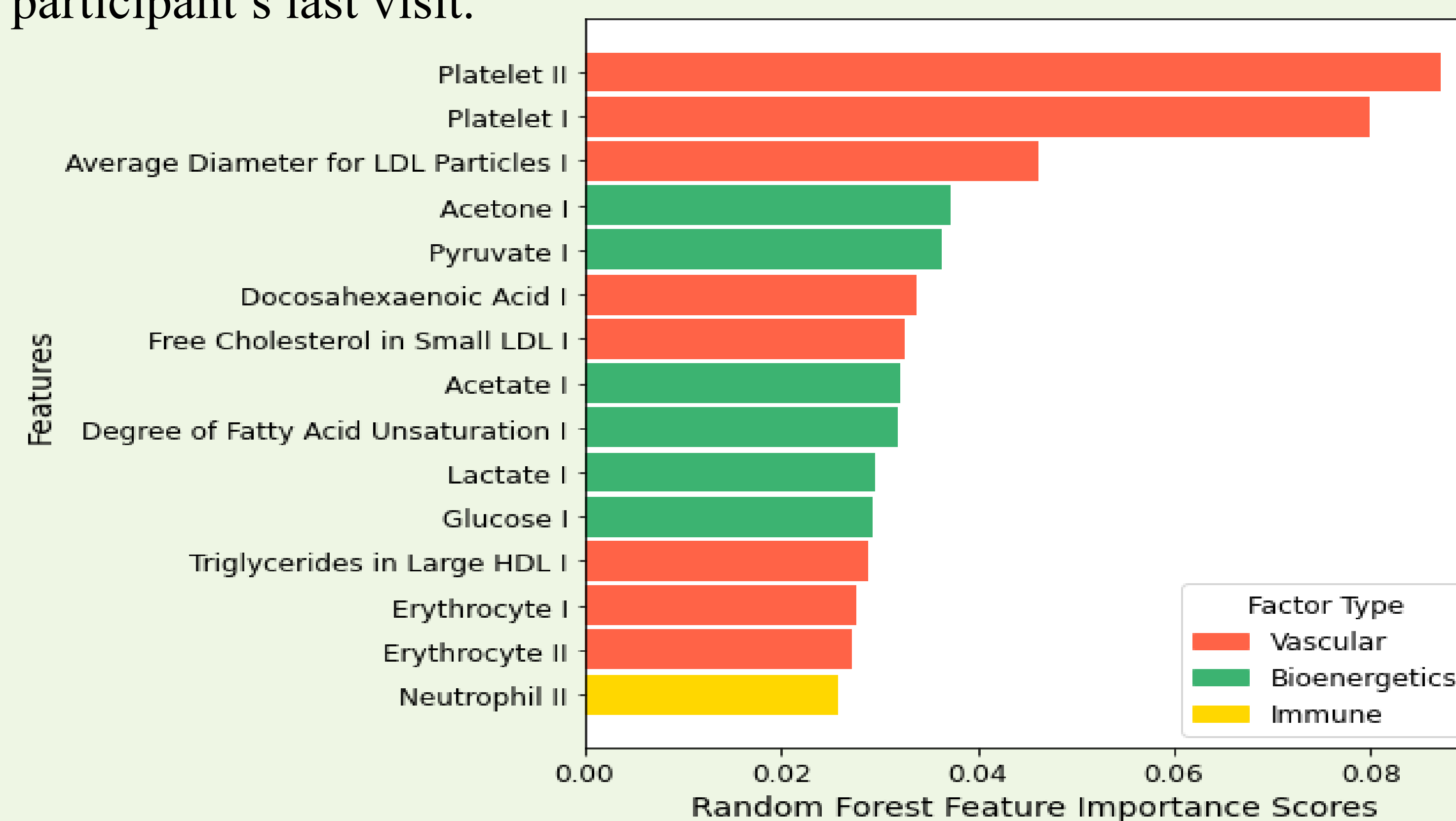
### Analysis and Results

- the RF model achieved an accuracy of 62%, sensitivity of 60%, specificity of 65%, precision of 77%, AUROC of 63%, and F-score of 67%. **Fig. 1** shows the ROC curve of the Random Forest model.



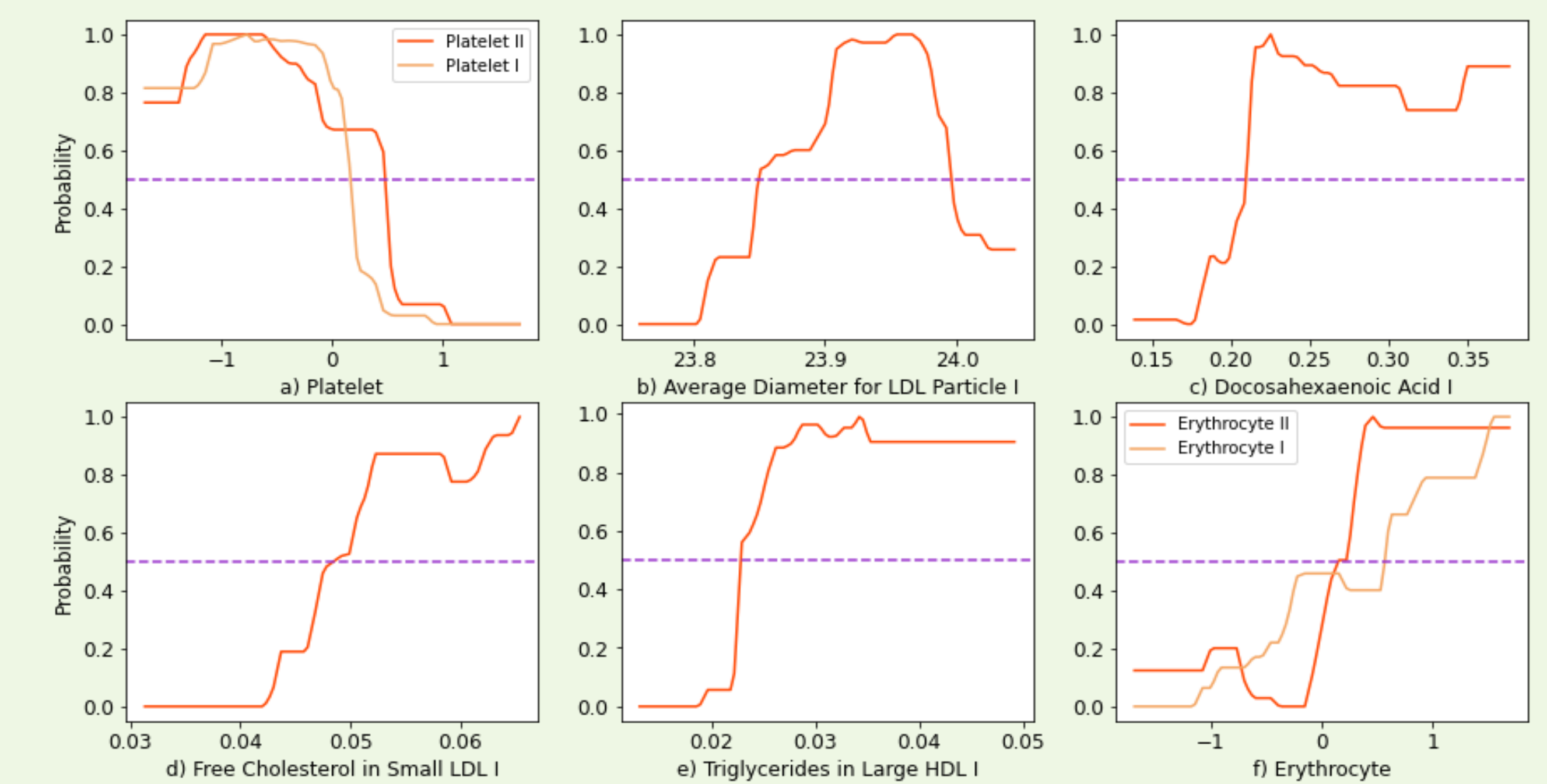
**Fig.1 .** Receiver Operation Characteristic (ROC) curve for predicting Positive-Ager vs. Cognitive Decliner groups

- RF model provided feature importance ranking that suggests which variables best distinguish between cognitive trajectory groups. **Fig. 2** illustrates the top fifteen important features. The "I" and "II" symbols represent variables collected either at baseline or on a given participant's last visit.

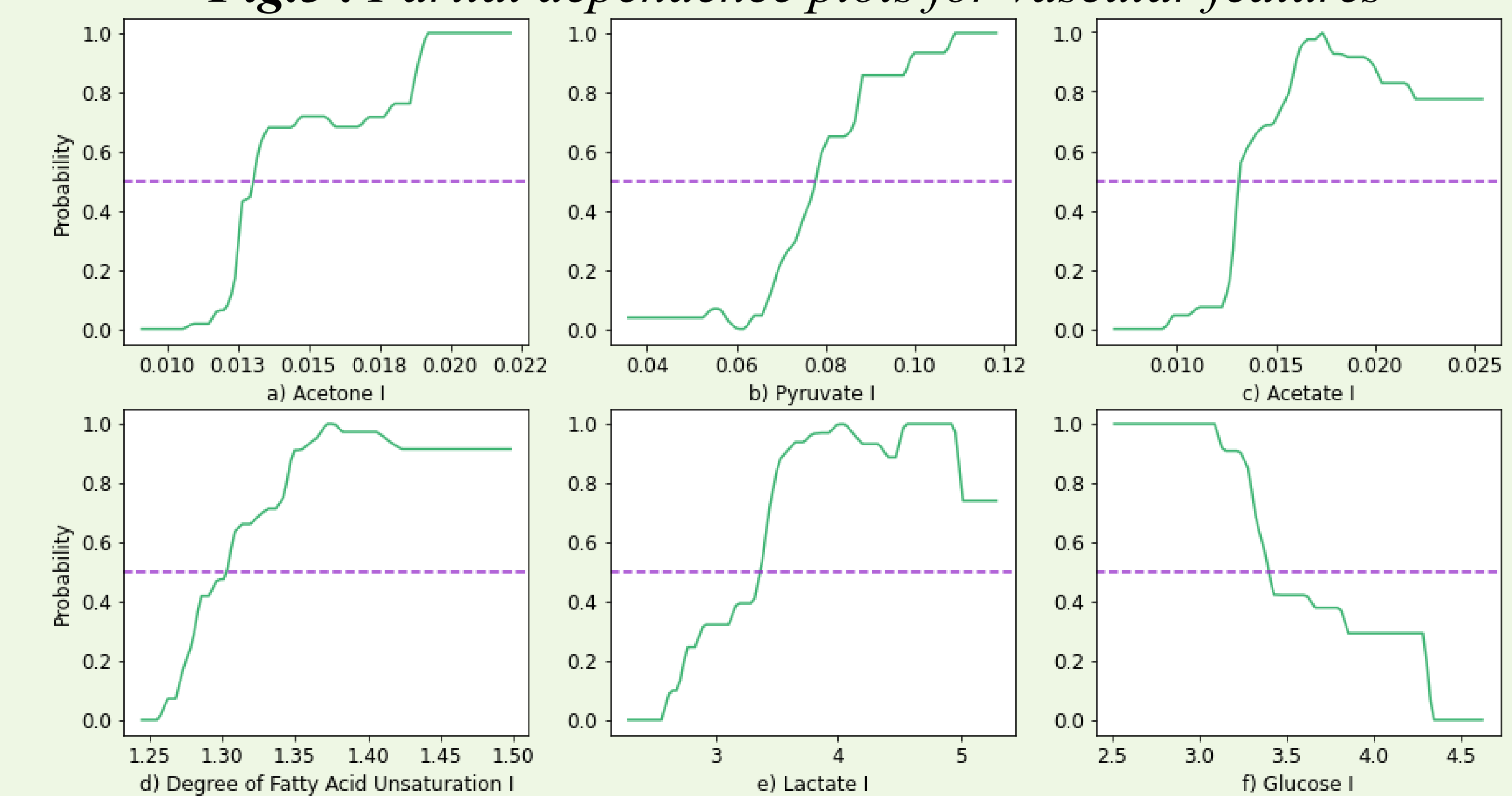


**Fig.2 .** Feature importance ranking for the top fifteen features. Vascular and bioenergetics factors showed equal contribution in the cognitive trajectory type prediction.

- Partial dependence plots show how levels of feature, marginalized over all other features, predict who is in the Positive-Aging group vs. Cognitive Decline group. The y-axis shows the predicted probability of being either in the Cognitive Decline group (0-0.49) or Positive-Aging group (0.5-1.0). This probability varies as a function of the individual variable (x-axis).



**Fig.3 .** Partial dependence plots for vascular features



**Fig.4 .** Partial dependence plots for bioenergetics features

### Conclusion

- The model found that an equal combination of vascular and bioenergetics factors could modestly explain differences in cognitive trajectories over 7-9 years.
- Prediction of cognitive trajectory types in late-life with various factors of mid- and late-life would be a novel and valuable step to mitigate cognitive decline in normal aging and Alzheimer's disease.
- Modifiable health biomarkers in mid-life are more important in cognitive aging than static factors such as age and sex.
- **Submitted to Geroscience (official journal of the American aging association)**