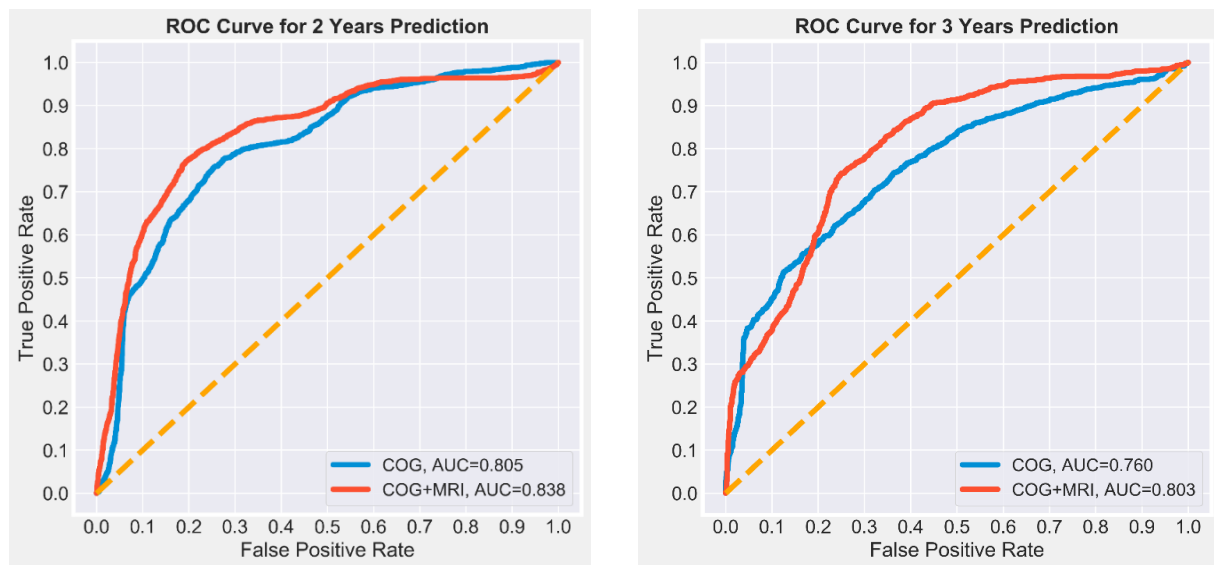


# Supplementary Material

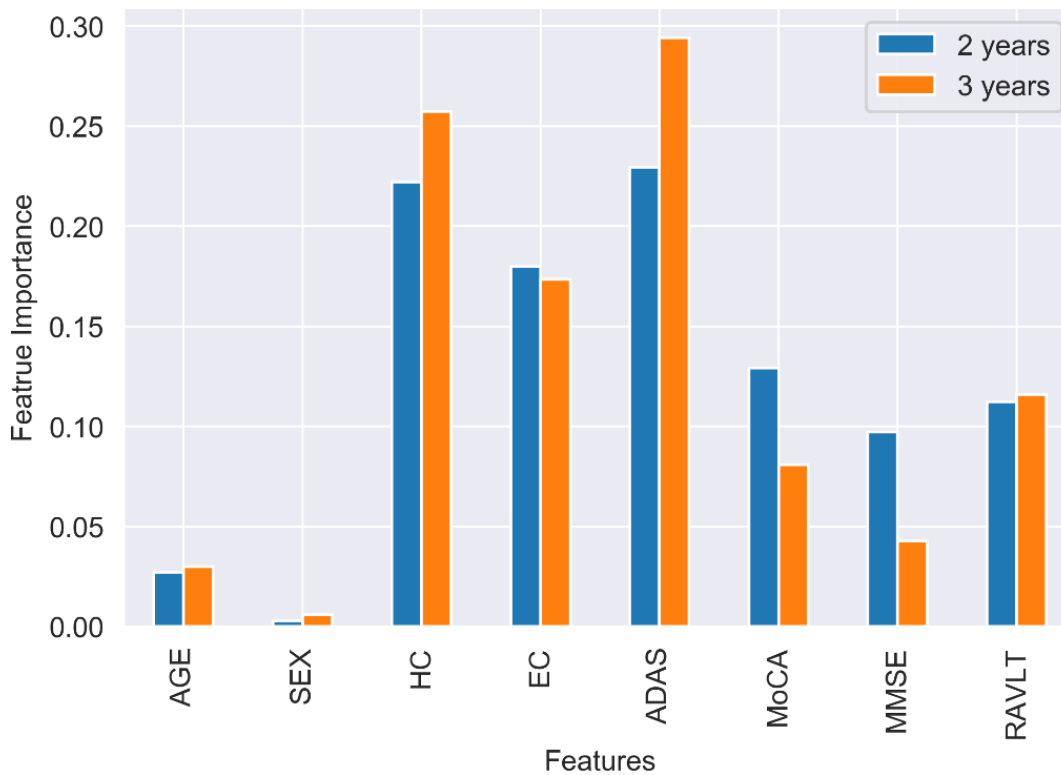
## Automatic Prediction of Cognitive and Functional Decline Can Significantly Decrease the Number of Subjects Required for Clinical Trials in Early Alzheimer's disease

To ensure that the imbalance in the data does not bias the results, we also reported the AUC for each of the models and demonstrated the ROC curve for two models: One consisting of all cognitive features and the other using both cognitive and MRI features (Supplementary Figure 1).



Supplementary Figure 1. ROC curve of the model for both follow-up periods

Supplementary Figure 2 shows the importance of each feature for both follow-up periods, showing how much each of these features affect prediction accuracy. To calculate the importance, we used the mean decrease of the impurity [1]. The impurity decrease for each of these features were averaged over all the nodes in all of the trees, using the Gini index as the impurity measure. In both models, ADAS is the most important feature followed by SNIPE scores for HC and EC. At three years, both ADAS and HC SNIPE gain importance while the two other cognitive scores fall behind. The increase in the importance of the SNIPE scores in time, shows its ability to detect AD-related changes earlier than most cognitive scores. The lowest importance was achieved for age and sex comparing to other features. We further tested for the significance difference of the feature importance between the two follow-up periods. The correction for multiple comparison showed the difference for all features is significant, except for EC and RAVLT.



**Supplementary Figure 2.** Feature importance for both follow-up periods

**REFERENCE**

[1] Louppe G, Wehenkel L, Sutura A, Geurts P (2013) Understanding variable importances in Forests of randomized trees. *Advances in Neural Information Processing Systems 26 (NIPS 2013)*, Burges CJC, Bottou L, Welling M, Ghahramani Z, Weinberger KQ, eds