The Potential for MRI-based Predictive Modelling for Treatment Prioritization and Clinical Trials

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BACKGROUND

- Treatments in Alzheimer's disease (AD) are moving towards earlier stages of disease, notably MCI and preclinical AD. This population demonstrates a high degree of variability in illness progression – increasing costs and masking treatment effects during clinical trials.
- Artificial Intelligence and predictive modelling approaches, such as QyPredict®, can enable the integration of clinical, demographic, genetic, and neuroimaging to enrich clinical trial samples with patients who will experience cognitive decline.
- Previously, we have presented the application of QyPredict to enrich clinical trials in an **MCI and AD population**, achieving a balanced accuracy of 72%, sensitivity of 70%, specificity of 73%, and a positive predictive value of 80% (Gordon et al., 2023).
- We modelled a **preclinical AD and MCI** placebo group and investigated the effects of clinical trial enrichment using QyPredict®.

METHODS

- Using data from ADNI, OASIS, NACC, and A4, a clinical trial placebo group (n = 674) was modelled with the following criteria: Diagnosis: MCI or preclinical AD, Age: 55-85 years, MMSE: 24-30, Amyloid Status: Positive, APOE4 Status: negative or heterozygous.
- Using QyScore® volumetric MRI measures, and standard demographic and clinical data, QyPredict® was applied to enrich the modelled clinical trial placebo group for future decliners. Patients were classified as either Predicted Decliners or Predicted Stables, with cognitive decline, defined as an increase in CDR-SB >0.5 over 24 months.
- Cognitive decline was compared before and after the application of QyPredict®.

QYPREDICT® RESULTS IN PRECLINICAL AD AND MCI

- QyPredict® accurately predicted future cognitive decline, achieving a balanced accuracy of 69%, sensitivity of 64%, and a specificity of 73%.
- QyPredict® removed 73.7% of Stable patients from the modelled placebo group (**Figure 1**), resulting in a statistically significant (p < .001) 100% increase in detected cognitive decline by 24 months (**Figure 2** and **Table 2**).

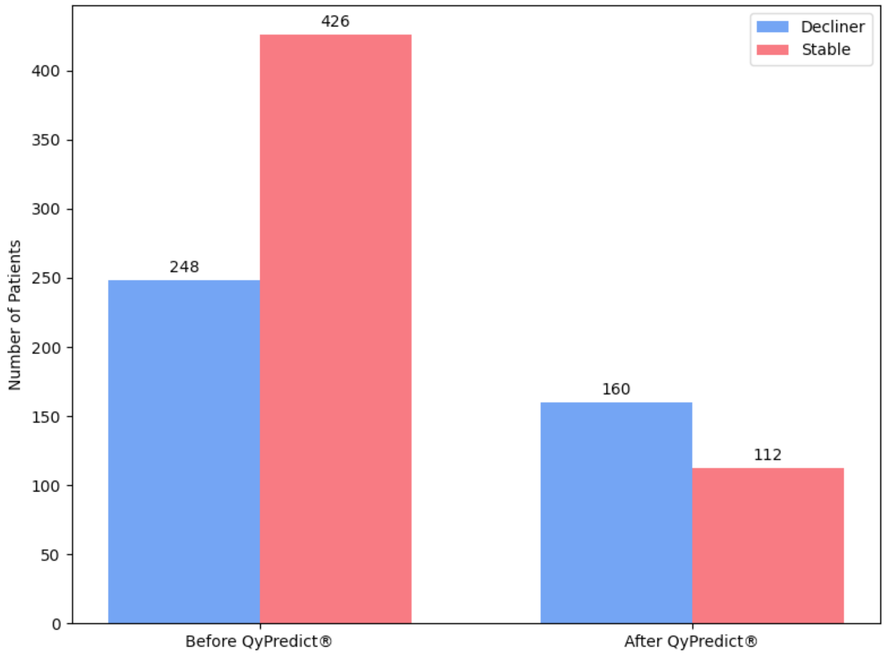

Figure 1. Shows the proportions of true Decliners and true Stables in the modelled clinical trial placebo group, before and after the application of QyPredict®.

Table1. Shows change in cognitive decline before and after applying QyPredict® to a modelled clinical trial placebo group.

Timepoint	**Before** QyPredict® 24 month CDR-SB Change	**After** QyPredict® 24 month CDR-SB Change
12 months	0.21	0.38
24 months	0.45	0.90

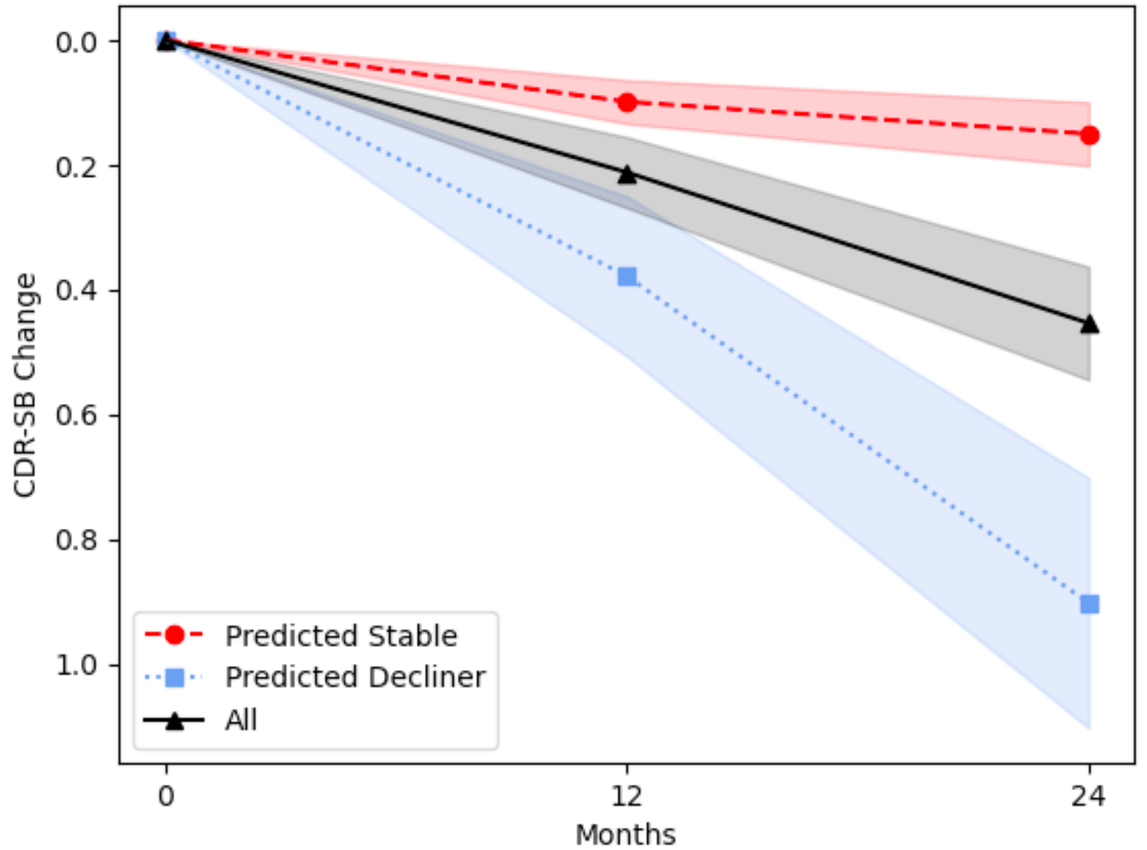

Figure 2. Shows the cognitive decline of Predicted Decliners and Predicted Stables over 24 months QyPredict®.

CONCLUSIONS

- QyPredict®'s accuracy in these earlier stages of disease are consistent with previous work showing QyPredict's accuracy in patients with more advanced disease.
- QyPredict® can drastically improve a clinical trial's ability to detect a treatment effect, by better selecting patients who will experience cognitive decline during the trial.
- QyPredict® has the potential to drastically improve clinical trial outcomes in preclinical and early AD, with further development utilising more real-world clinical trial data for validation.