QYPREDICT® PROGNOSTIC MODEL ENRICHES ENROLMENT FOR FASTER DECLINERS IN MILD COGNITIVE IMPAIRMENT

Elizabeth Gordon[1], Luca M. Villa[1], Jorge Samper-Gonzales[1], Thomas Jubault[1], Nicolas Guizard[1], the Alzheimer's Disease Neuroimaging Initiative

[1]Qynapse, 2-10 rue d'Oradour-sur-Glane, 75015 Paris, France

BACKGROUND

- The suboptimal selection of patients is a key challenge for disease-modifying clinical trials in mild cognitive impairment (MCI) and Alzheimer's disease.
- Improved selection strategies are urgently needed to better power trials.
- Recent advances in AI predictive modeling, such as the QyPredict® algorithm, are promising tools to improve the selection of patients likely to clinically progress during the timeframe of a clinical trial.

OBJECTIVES

- To predict patients that would show cognitive decline or remain stable in a simulated clinical trial placebo group, over a 24-month period, in order to produce a simulated enriched patient cohort.

METHODS

- QyPredict® was applied to 677 MCI and AD patients from ADNI, OASIS, and NACC: age: 72.4 ±7.0, 41.8% female, MMSE range 24-30, who had either amyloid positive or APOE-ε4 positive status.
- QyPredict®, a tunable machine learning model, incorporated baseline QyScore® volumetric MRI measures, demographic and clinical (Sex, MMSE and CDR) inputs.
- A QyPredict® probability value (0-1) was produced for each individual, representing the probability they would demonstrate a modelled cognitive decline – defined as an increase in CDR-SB of >0.5 over 24 months. An additional analysis predicting MMSE decline over 24 months was also conducted.
- Predictive performance was evaluated using balanced accuracy, sensitivity, specificity, and positive predictive value.
- Actual change versus predicted change in CDR-SB scores was further investigated for 'Stable' (QyPredict® probability value <0.5) versus 'Decliners' (QyPredict® probability value >0.5).
- Sample sizes to detect a 30% treatment effect (reduction in change in CDR-SB) were calculated for the full sample and an enriched cohort with only 'Decliners'.

RESULTS

- For the full sample without QyPredict® enrichment, change in CDR-SB at 24 months was 1.1, which significantly increased ($p < .001$) from a QyPredict® probability value >0.5, reaching a change of 1.9 points.

Figure 1. Observed change in CDR-SB score for All Participants, Predicted Stable, and Predicted Decliners, across the Full Cohort (A), Aβ Positive Cohort (B), and APOE-ε4 Positive Cohort.

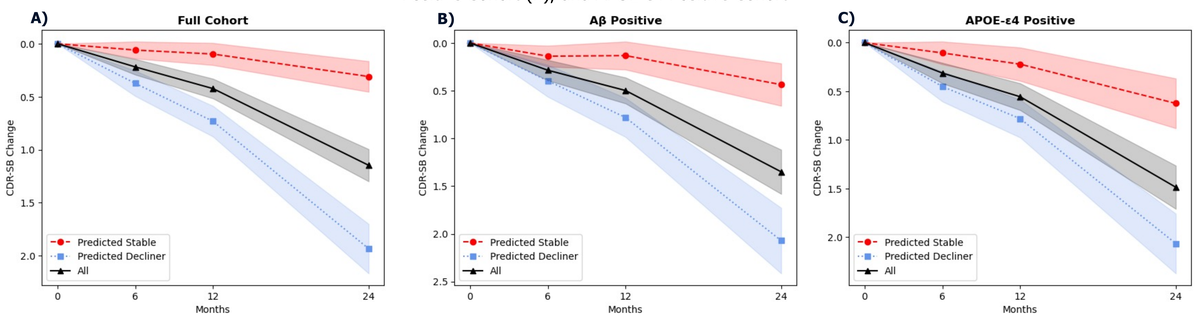

Table1. Shows estimated sample sample size reduction (per treatment arm) due to cohort enrichment.

Desired Clinical Trial Treatment Effect	Sample Size Reduction Due To Cohort Enrichment		
	Full Cohort	Aβ positive Cohort	APOE-ε4 Positive Cohort
30% Treatment Effect	59%	48%	41%

Figure 2. Shows a spider plot of performance metrics for predicting CDR-SB change over 24 months, across the Full Cohort.

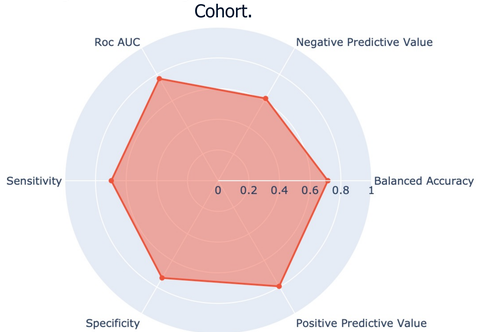

Table2. Shows performance metrics across all prediction models.

	Balanced Accuracy	Sensitivity	Specificity	Positive Predictive Value
Full Sample				
CDR-SB Change - 24 Months	0.72	0.70	0.73	0.80
MMSE Change - 24 Months	0.65	0.64	0.67	0.48
Aβ Positive				
CDR-SB Change - 24 Months	0.68	0.67	0.69	0.80
APOE-ε4 Positive				
CDR-SB Change - 24 Months	0.68	0.71	0.65	0.81

CONCLUSIONS

Using baseline QyScore® metrics, basic demographic, and typical clinical data, commonly available at screening visits, QyPredict® successfully modelled future cognitive decline, resulting in a substantially reduced enriched patient cohort required to detect a positive treatment effect.