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

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Qynapse

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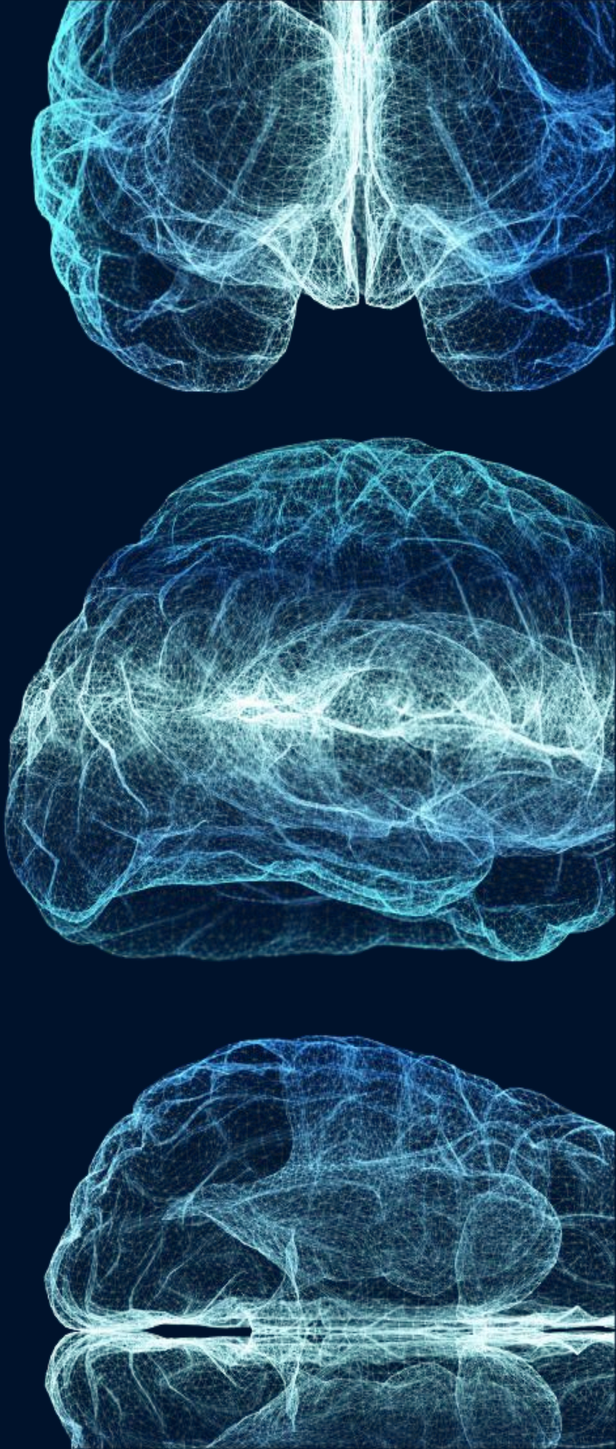

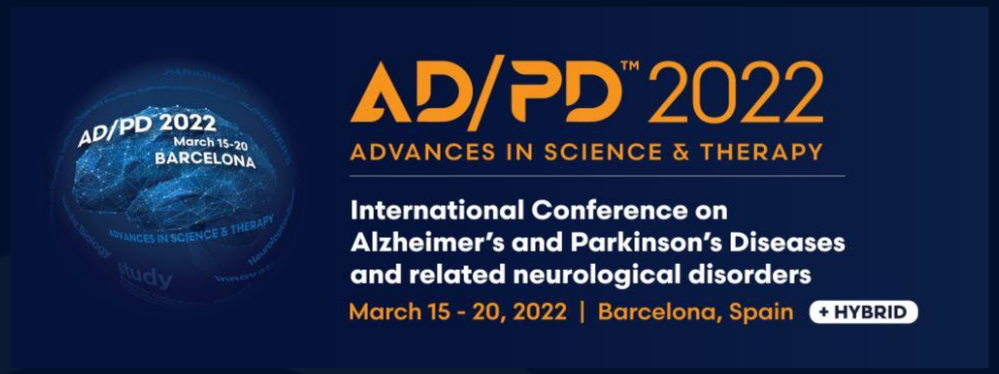

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DISCLOSURES

	Nothing to disclose
X	Yes, please specify

Company Name	Honoraria / Expense	Consulting / Advisory Board	Funded Research	Royalties / Patent	Stock Options	Ownership / Equity Position	Employee	Other (Please specify)
Qynapse							X	

Background

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Key Challenges:

- Many patients enrolled in clinical trials for Alzheimer's Disease (AD) interventions do not progress clinically over the study period, reducing the power to detect positive treatment effects.
- The increased heterogeneity and slower decline in mild cognitive impairment (MCI) pose even greater challenges but this stage is a better window to target intervention.
- The suboptimal selection of patients has been a key contributor to the reduced success rate of disease-modifying trials and improvements in selection strategy are urgently needed to better power clinical trials.

New Approaches:

- Recent advances in AI predictive modeling, such as the QyPredict® algorithm, are promising tools to improve the selection of patient populations more likely to clinically progress during the timeframe of an AD clinical trial.

Study objectives

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1. To evaluate the prognostic value of QyPredict® in all-comer mild cognitive impairment (MCI) populations as well as amyloid-positive (Aβ+) and APOE-ε4 + sub-populations.

2. To evaluate the benefit of using QyPredict® to refine patient selection in terms of clinical trial success probability in a simulation study.

INTRODUCTION
QYPREDICT®

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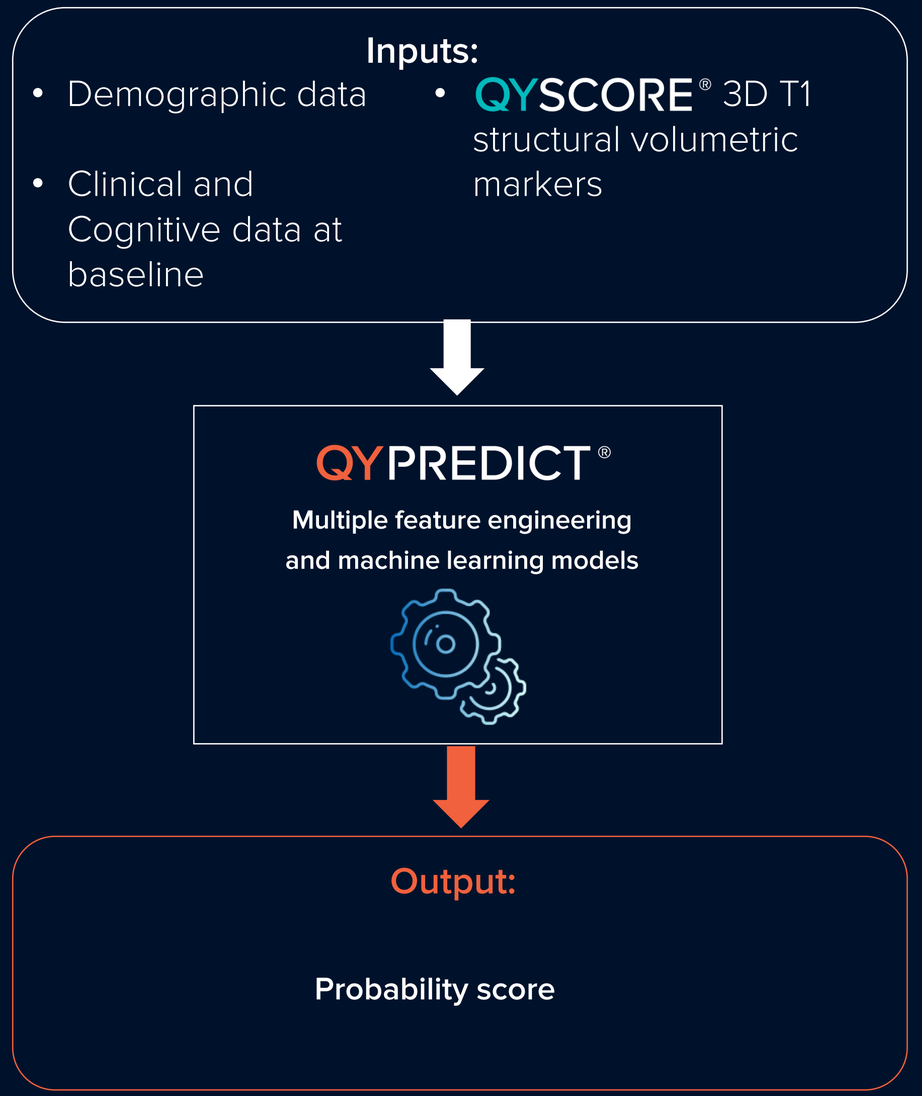
What is QyPredict®?

- QyPredict® is a prognostic model currently developed for use in mild cognitive impairment (MCI) populations

- QyPredict® takes different **baseline** inputs : structural MRI outputs from QyScore®, demographic and clinical data, genetic and biological disease markers



INTRODUCTION
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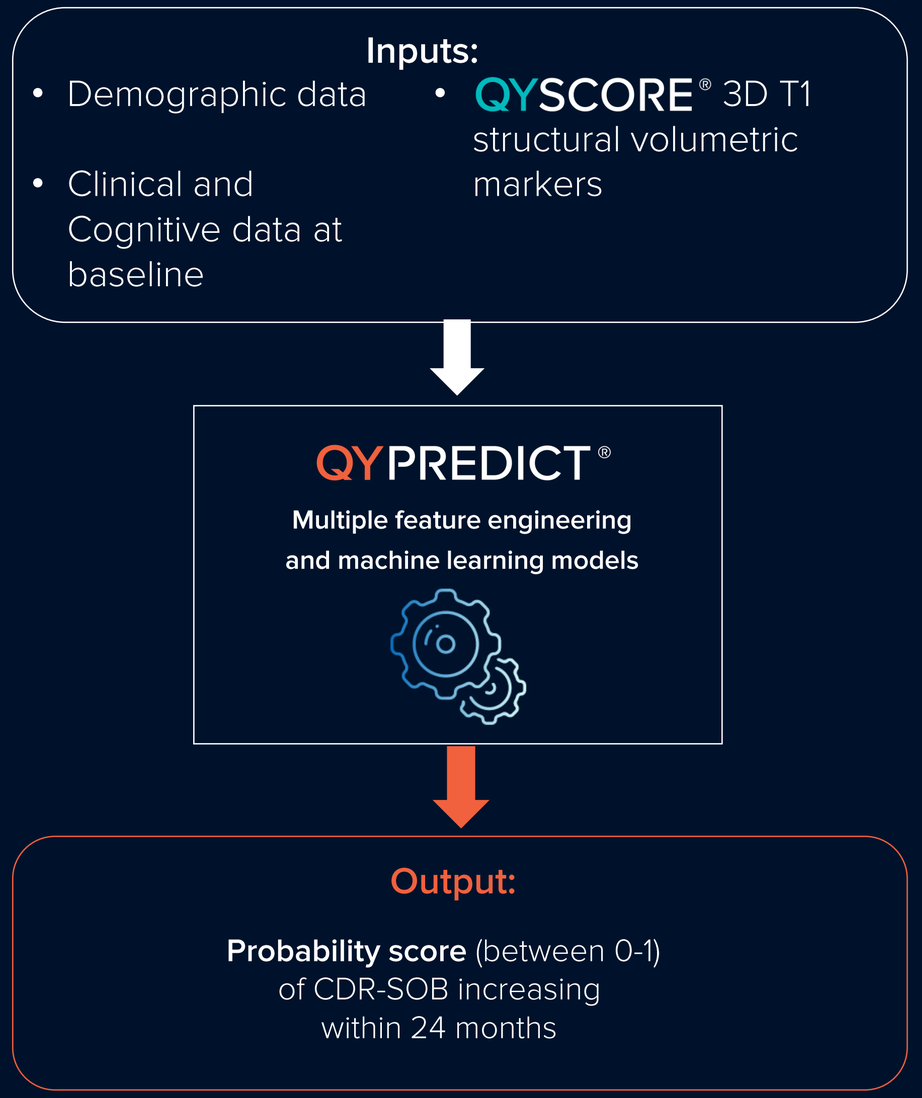
What information does QyPredict® provide?

- For each individual, QyPredict® generates a score (between 0-1) representing a probability of having a specific outcome (e.g. an increase of at least 0.5 points of CDR-SOB score over 24 months)

- Allows for a personalized medicine approach by providing prediction on an individual patient level



Methods

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Participants

Study participants were from **ADNI** with the following inclusion criteria:

- Age (55 – 85 years of age)
- MCI diagnosis
- MMSE between 24 and 30
- CDR = 0.5 at baseline
- Available amyloid status

Methods

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Analyses

- A QyPredict® probability of decline was calculated for each of the 519 individuals modeled **over 24 months.**
- The performance of QyPredict® to accurately model real decline in CDR-SOB was evaluated at several **increasing probability of decline cut-offs of 0.1, 0.2, 0.3, 0.4 and 0.5.**
- For the total cohort, Amyloid+ and APOE-ε4+ populations, the mean, standard deviation and Cohen's d for CDR-SOB change was calculated.
- Sensitivity, specificity, positive predictive value (PPV) and power calculations were computed to assess predictive performance.
- Finally, a clinical trial simulation was run to further investigate the utility of QyPredict® to improve the probability of clinical trial success.

Results

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Demographics and CDR-SOB for the Full and filtered QyPredict® Cohorts

- Age increased with increasing QyPredict® threshold (*p<0.001* only for QyPredict® > 0.4)
- Baseline CDR-SOB increases but it is only significant when comparing the full and QyPredict® > 0.5 groups
- Change in CDR-SOB significantly increased based on the baseline QyPredict® values
- Proportion of Amyloid positive individuals increases above QyPredict® of 0.2

Cohort	N	Age	Sex (M/F)	CDR-SOB at baseline	CDR-SOB at 12 months	CDR-SOB at 24 months	Amyloid positive N (% total)	APOE-ε4 status (+ / -) (% +)
Full cohort	519	71.8 (±7.1)	303 / 216	1.5 (±0.90)	1.8 (±1.38)	2.3 (±2.11)	319 (61%)	263 / 256 (51%)
QyPredict® > 0.1	467	72.2 (±7.0)	287 / 180	1.6 (±0.91)	1.9 (±1.39)	2.5 (±2.14)	300 (64%)	243 / 224 (52%)
QyPredict® > 0.2	418	72.6 (±7.0)	266 / 152	1.6 (±0.90)	2.0 (±1.4) *	2.7 (±2.17) *	283 (67%) *	223 / 195 (53%)
QyPredict® > 0.3	353	73.2 (±6.8)	224 / 129	1.6 (±0.93)	2.2 (±1.41) *	3.0 (±2.21) *	257 (72%) *	195 / 158 (55%)
QyPredict® > 0.4	313	73.4 (±6.6) *	199 / 114	1.7 (±0.95)	2.3 (±1.42) *	3.1 (±2.25) *	234 (74%) *	179 / 134 (57%)
QyPredict® > 0.5	251	73.9 (±6.6) *	154 / 97	1.7 (±0.97) *	2.4 (±1.44) *	3.4 (±2.30) *	197 (78%) *	148 / 103 (59%)

Results: Stable versus Decliners

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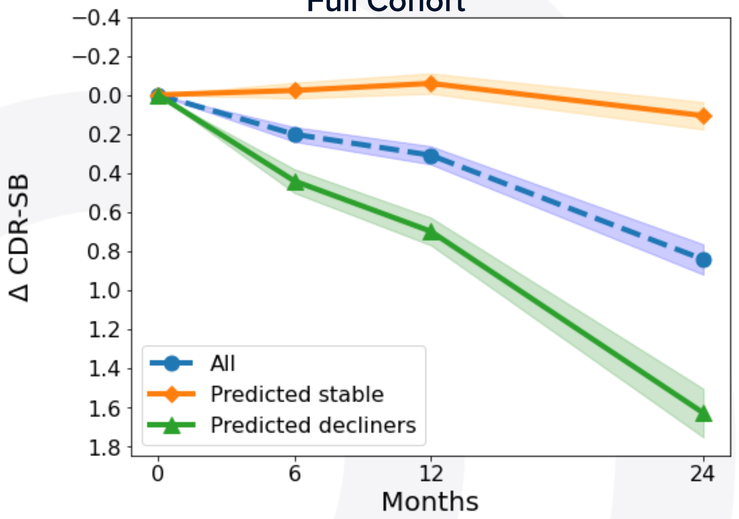
- QyPredict® performed well at predicting those that would decline and those that would remain stable over 24 months in all Cohorts.
- Stable defined as a QyPredict® score < 0.5 and Decliner as QyPredict® > 0.5

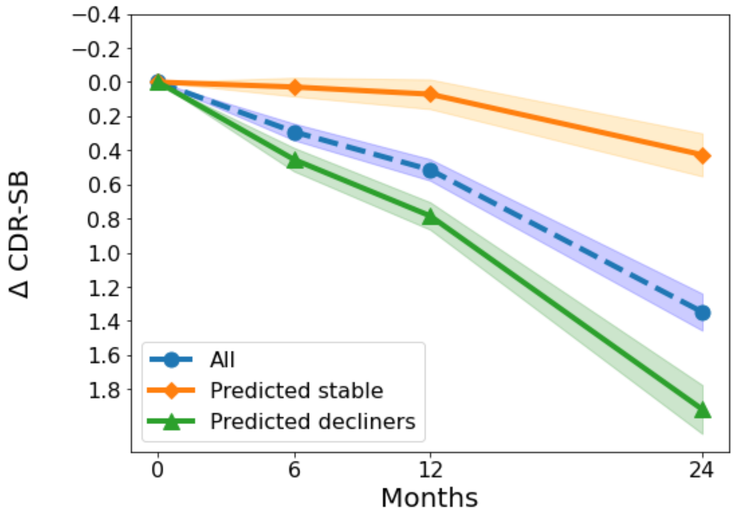
Full Cohort



251 subjects were predicted to decline.
190 actually declined, for a **PPV*** of **0.76**, **sensitivity** of **0.7** and **specificity** of **0.75**

Sample size	Un-Enriched Cohort	Enriched Cohort
30% treatment effect	304	102
50% treatment effect	111	38

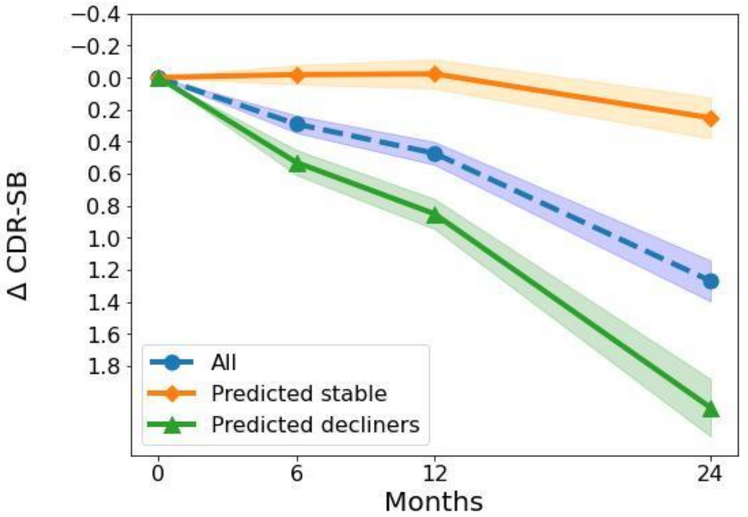
Amyloid +



197 subjects were predicted to decline.
164 actually declined for a **PPV** of **0.83**, **sensitivity** of **0.77** and **specificity** of **0.70**

Sample size	Un-Enriched Cohort	Enriched Cohort
30% treatment effect	144	77
50% treatment effect	53	29

APOE-ε4 +



148 subjects were predicted to decline.
122 actually declined for a **PPV** of **0.82**, **sensitivity** of **0.75** and **specificity** of **0.74**

Sample size	Un-Enriched Cohort	Enriched Cohort
30% treatment effect	184	79
50% treatment effect	68	30

* PPV = positive predictive value

QYPREDICT® and **Clinical Trials Simulation**

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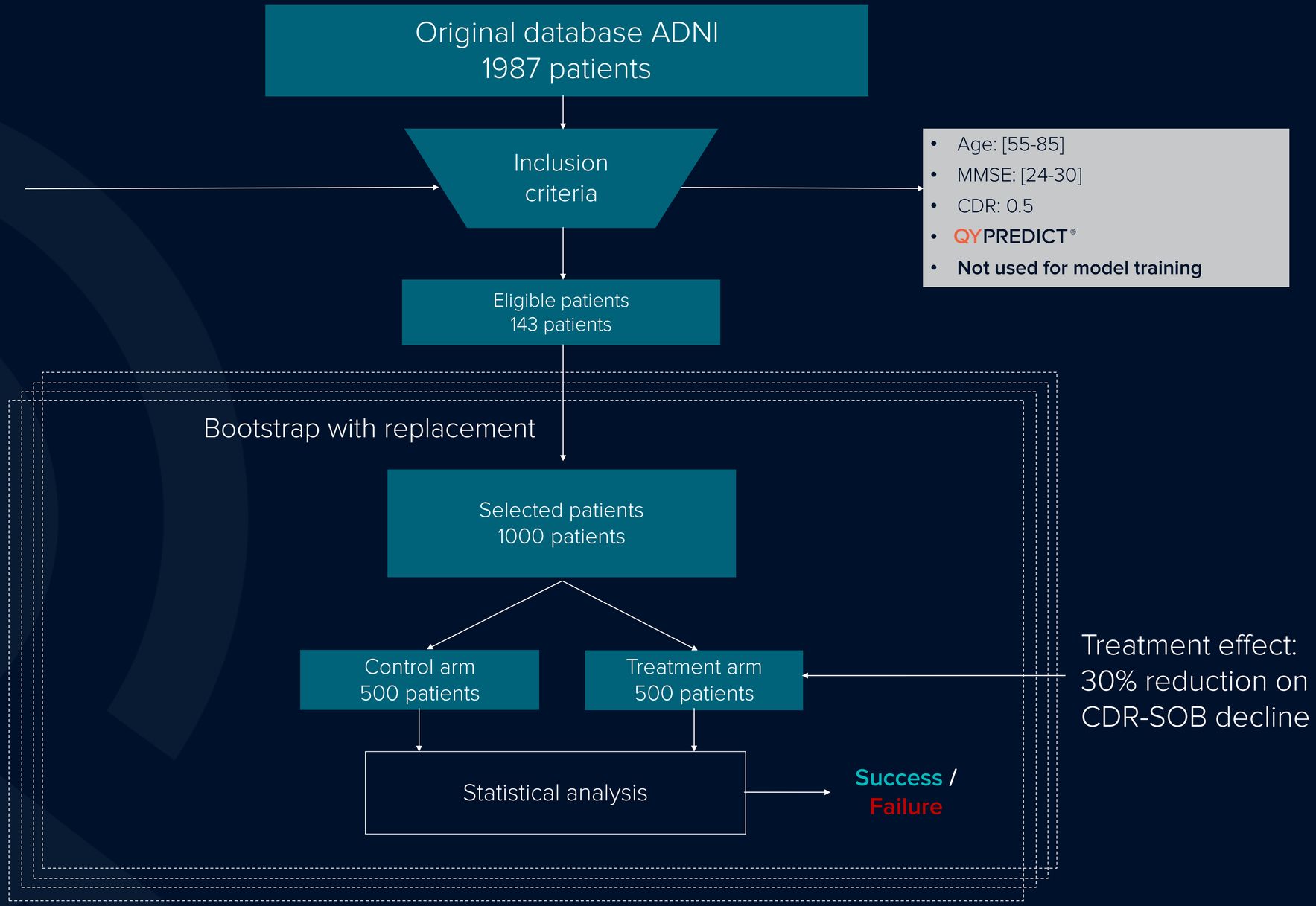
QYPREDICT® incorporated into the inclusion criteria at screening



Repeated for 1000 simulations

Treatment effect: 30% reduction on CDR-SOB decline

Clinical Trial **Simulation Results**

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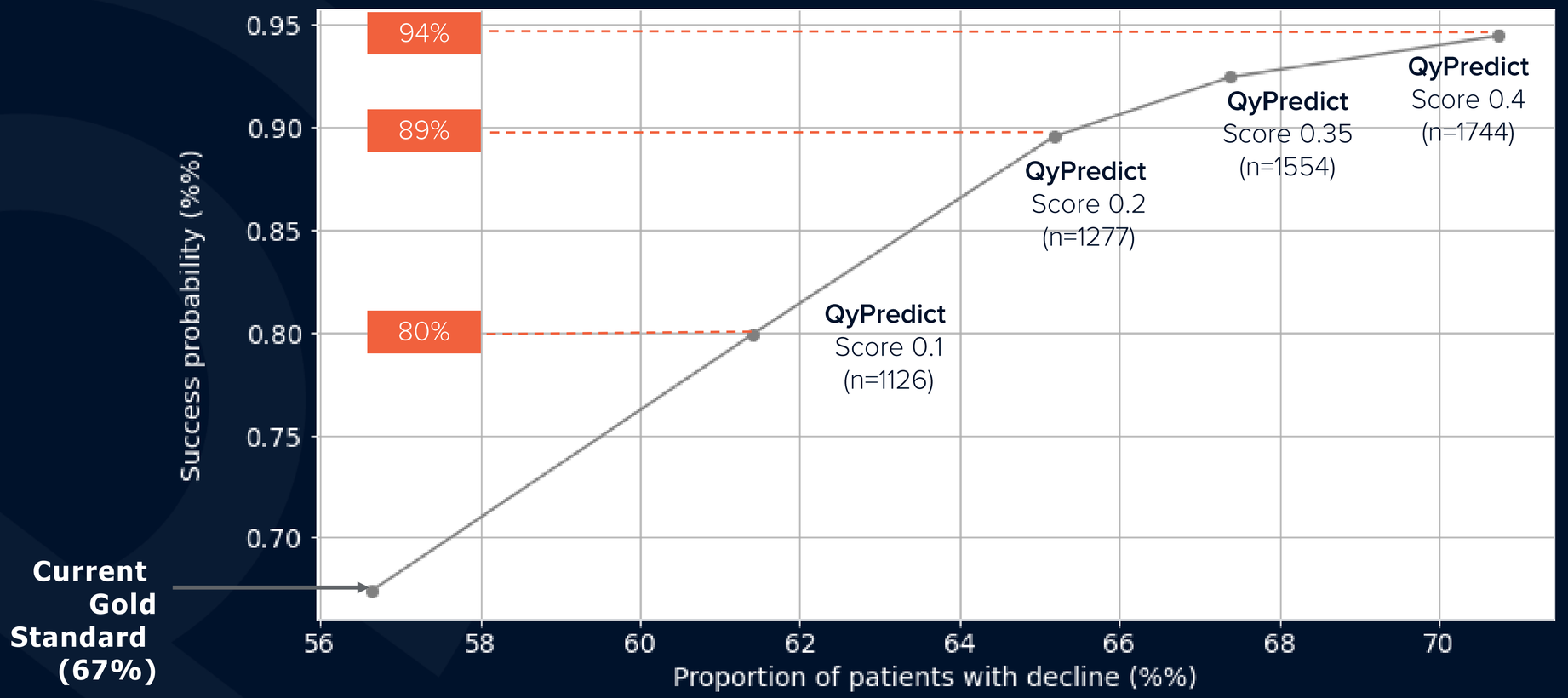
QYPREDICT® incorporated into the inclusion criteria at screening



n = total patients screened to reach 1000 patients enrolment

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SUMMARY AND CONCLUSIONS

- Using baseline neuroimaging and demographic information, QYPREDICT® was able to accurately model the likelihood an individual patient would decline over 24 months in all-comers, Amyloid positive and APOE positive populations, based on change in CDR-SOB.
- Sensitivity, specificity and positive predictive value where high across the different populations (all > 0.70).
- Enriching using QYPREDICT® substantially reduced sample sizes required to detect a treatment effect.

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SUMMARY AND CONCLUSIONS

- QYPREDICT® shows promise in improving trial selection towards decliners for increased trial success probability with a single upfront screening cost.

- The use of QYPREDICT® score as part of the inclusion criteria in our clinical trials simulation **significantly** improved the probability of trial success, while increasing screening failure rates due to excluding those who would be less likely to clinically progress.

- These results support the promising potential to improve design and power of AD clinical trials, and the likelihood of **detecting positive treatment effects** and **achieving trial success.**

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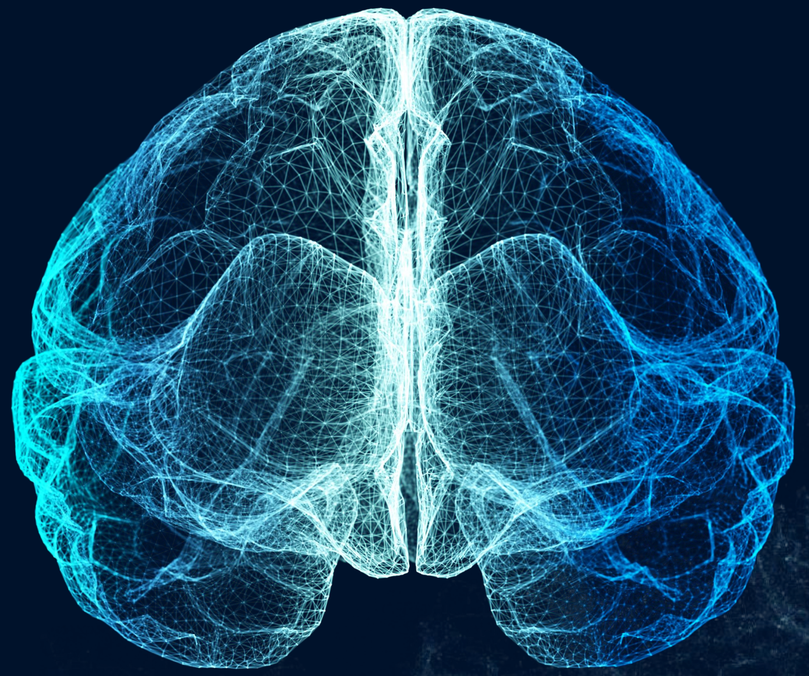
THANK YOU FOR YOUR ATTENTION AND I WELCOME ANY QUESTIONS



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PEACE OF MIND