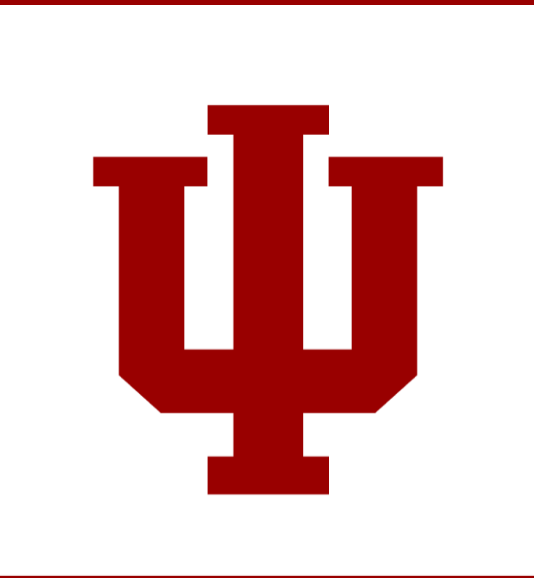




A Brief Telephone Memory Test for Efficient Cognitive Screening in Dementia Research

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Background

Remote cognitive screening is increasingly important for dementia research, particularly for identifying individuals who may benefit from in-person neuropsychological evaluation, plasma biomarker testing, amyloid-PET, or clinical trial referral.

Plasma biomarkers such as p-tau217 provide valuable information about Alzheimer’s disease risk, but no not characterize current clinical impairment. Brief telephone assessment of memory and subjective cognitive concerns may provide a low-burden measure of cognitive phenotype that complements biomarker-based risk assessment.

Objective

To evaluate whether a brief telephone-based memory test can support efficient cognitive screening and triage in dementia research by:

- 1. Distinguishing clinical diagnostic groups.
- 2. Enriching for amyloid-PET positivity.
- 3. Adding predictive value to plasma p-tau217 and cognitive concerns for identifying clinical mild cognitive impairment (MCI).

Study Sample

The sample was drawn from the Indiana Memory and Aging Study (IMAS) embedded within the Indiana Alzheimer’s Disease Research Center (IADRC) cohort. Telephone screening for IADRC participants includes administration of a 10-item word list learning and recall test [1]. Delayed recall data from this task was matched with clinical diagnosis and detailed neuropsychological battery performance from an in-person baseline visit completed within 30 days of screening. Baseline assessment included the NACC Uniform Data Set (UDSv3) plus Rey Auditory Verbal Learning Test (RAVLT) [2] and this contributed heavily to the clinical adjudication of CU/MCI/AD dementia status. Performance on the telephone assessment did not inform clinical diagnosis in any way. Thus, RAVLT delayed recall performance was used as a criterion-linked benchmark against which the independent predictive utility of the telephone memory test could be evaluated.

Subsets of participant with a) amyloid-PET data within 12 months of screening, and b) p-tau217 plasma biomarker and self-reported memory concern (Cognitive Change Index, CCI) data collected within 6 months of screening were also extracted. Participants were characterized for presence or absence of subjective cognitive decline (SCD) based on a self-reported Cognitive Change Index (CCI-12, episodic memory items) score of ≥ 25 [3, 4].

Table 1. Sample size by study objective and participant characteristics

Objective	Details	N
1	CU	237
	MCI	99
	AD	23
2	Amyloid-PET Negative (Centiloids < 21)	108
	Amyloid-PET Positive (Centiloids ≥ 21)	36
3	CU (ptau217 & CCI subset)	135
	MCI (ptau217 & CCI subset)	40

Analyses

Objective 1. Models predicting MCI and AD versus CU status using phone screen or RAVLT delayed recall scores were compared using ROC/AUC.

Objective 2. Logistic regression models were fit to predict impairment status using phone screen delayed recall performance. Youden’s Index was used to define recall thresholds for optimizing MCI and AD status. These were then tested for their ability to enrich samples for A β -PET positivity by comparing the rate of positivity above baseline. Positive and negative predictive value (PPV/NPV) were also used to evaluate Amyloid-PET triage utility. Likelihood ratio tests (LRT) were used to test if phone screen offered predictive utility beyond p-tau217.

Objective 3. A baseline model predicting MCI using p-tau271 was compared with models including telephone delayed recall and/or cognitive complaint status using AIC, ROC/AUC, and nested model LRT. Repeated cross-validation was used to estimate internally validated AUC.

All models were covaried for age and sex

Telephone memory screening and self-reported memory concerns predict independently assessed clinical impairment. When paired with plasma p-tau217-measured biological risk, they improved identification of MCI in a scalable dementia research screening workflow.

Results: Distinguishing Clinical Groups

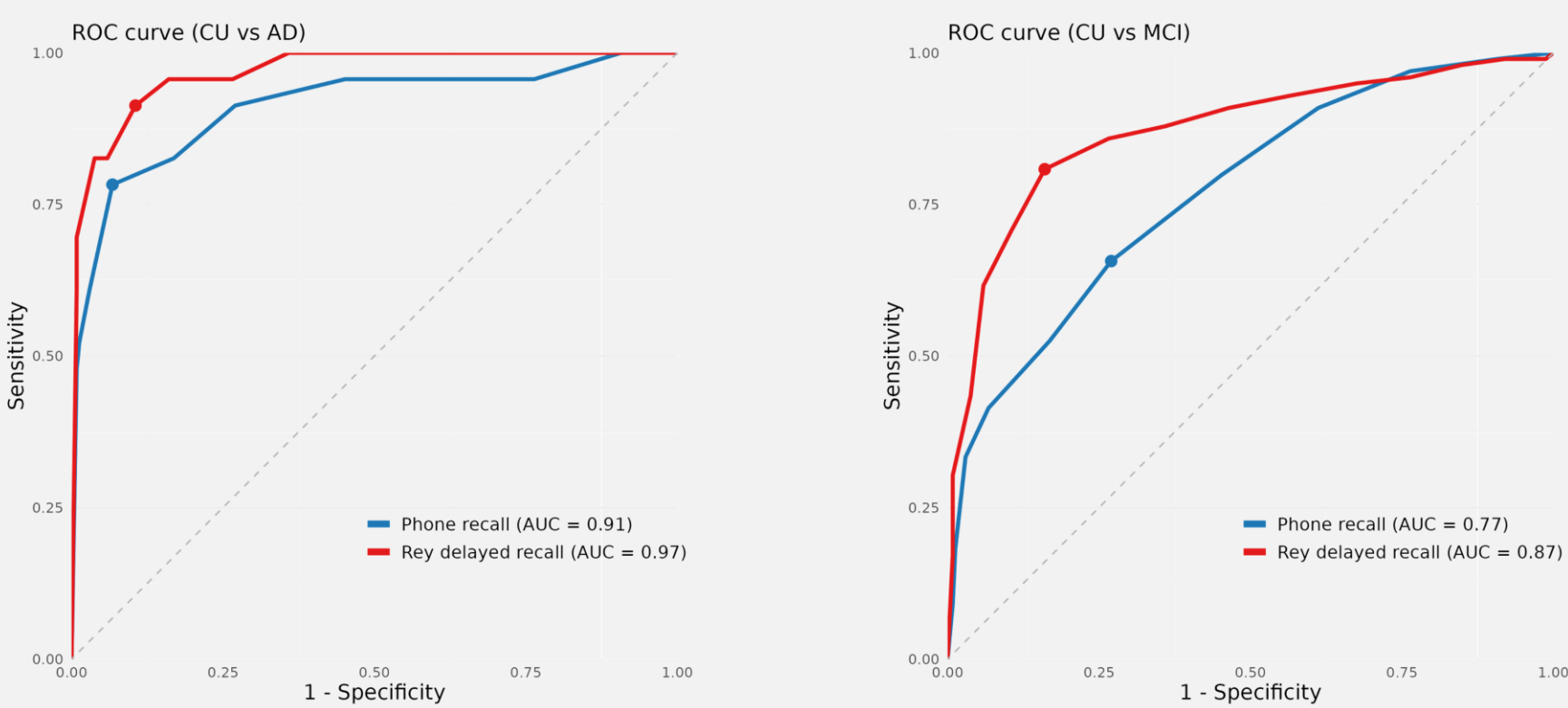


Fig 1. Models performed better when predicting AD (left) than MCI (right). RAVLT (red) was used to determine clinical diagnosis and provides a benchmark comparison for the phone test

References

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Results: Enriching for A β -PET Positivity

Table 2. Stricter thresholds improve PPV but cost NPV

Threshold	N Selected	PPV	NPV	Sensitivity	Specificity	Accuracy
5.5	61/144	34.40%	81.90%	58.30%	63.00%	61.80%
3.5	27/144	44.40%	79.50%	33.30%	86.10%	72.90%

Youden’s Index selected a threshold of 5.5 for capturing MCI participants and 3.5 for AD. The AD cutoff improved amyloid-PET yield but missed a substantial proportion of A β -positive individuals. Telephone memory screening may be useful for enriching research samples, but should not be used alone to rule out amyloid positivity. Among participants with both amyloid-PET and p-tau217 data, adding telephone memory performance and/or cognitive concern status did not improve prediction of A β -PET positivity (LRT $p > 0.5$).

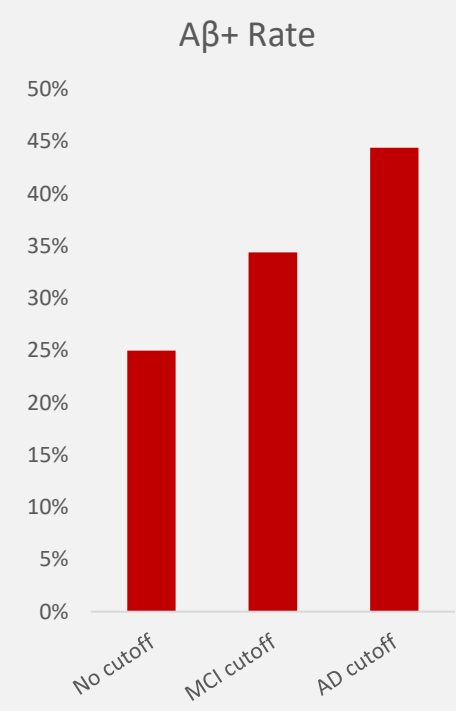


Fig 2. Phone-derived thresholds improve A β -PET positive yield over baseline (25%)

Results: Improving p-tau217 MCI Prediction

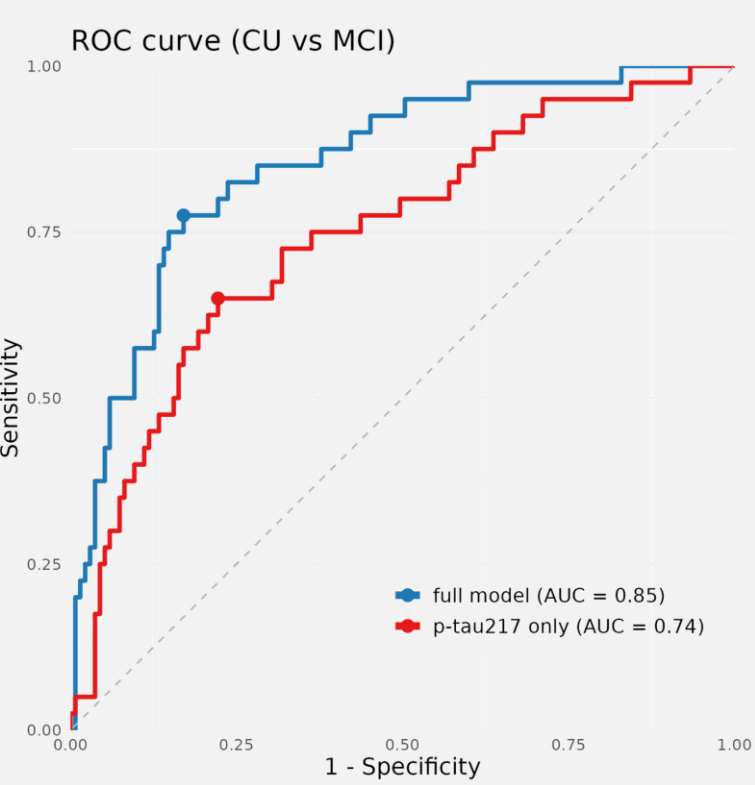


Fig 3. In-sample prediction of MCI with p-tau217 (red) improves with phone test and memory concerns on the CCI-12 (blue)

Table 3. Nested model comparisons selected the full model

	Model	AIC	LRT P	LRT Comparison
1	p-tau217	173	-	-
2	p-tau217 + mem.complaints	163	<0.001	Model 1
3	p-tau217 + phone	156	<0.001	Model 1
4	full (all the above)	149	0.003	Model 3

Table 4. Repeated cross-validation showed stable performance and substantial improvement in AUC

Model	Mean CV AUC	Median CV AUC	2.5%	97.5%
p-tau217	0.705	0.706	0.684	0.723
full	0.816	0.816	0.801	0.830
Delta	0.111	0.110	0.096	0.130

Conclusions

A brief telephone memory test provides clinically meaningful information for dementia research screening. RAVLT delayed recall showed stronger classification performance but was part of the clinical diagnostic information used to define clinical categories. In contrast, the telephone memory test was independent, making its performance against this benchmark particularly relevant for screening utility.

The telephone memory test did not replace plasma p-tau217 for amyloid-PET prediction, and phone-derived thresholds were insufficient for amyloid rule-out. However, telephone memory performance and memory concerns on the CCI-12 improved identification of clinical MCI beyond p-tau217 and to levels comparable to the RAVLT benchmark (in-sample AUC = 0.85 vs 0.87). This work suggest a simple remote clinical workflow that may pair well with plasma biomarker assessment to effectively triage participants in dementia research.