

Utility of plasma NfL and p-tau 217 in an Australian Memory Clinic

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Background

Plasma biomarkers may improve diagnostic accuracy in dementia but are not yet routinely implemented in clinical practice.

Neurofilament light (NfL): protein in myelinated axons, levels elevated in neurodegeneration and axonal damage

Phosphorylated tau (p-tau): marker of tau hyperphosphorylation, a core neuropathology of Alzheimer’s Disease (AD)

Aims

1. Describe the characteristics of the initial cohort of participants recruited for the BOLD study
2. Describe the concentrations of the blood biomarkers (NfL, p-tau 217) across diagnostic categories
3. Evaluate the classification utility of the biomarkers
 - Plasma NfL: Neurodegenerative vs non-neurodegenerative
 - Plasma p-tau 217: Presumed underlying AD (AD dementia, amnesic MCI) vs non-AD

Methods

- Observational cohort study in public hospital memory clinic conducted within existing clinic workflows
- Participants/caregivers asked for informed consent and to have blood sample taken
- Biomarker levels measured used the Roche-Elecsys platform
- Data extracted from electronic medical record
- **Primary outcome:** Clinical diagnosis following multidisciplinary assessment blinded to biomarker result
- Descriptive statistics used to describe demographic characteristics of cohort
- Box and whisker plots used to describe biomarker concentrations across diagnostic groups
- Area under ROC curves used to describe the classification utility of the biomarkers, and Youden’s index used to identify optimal cut-off

Results

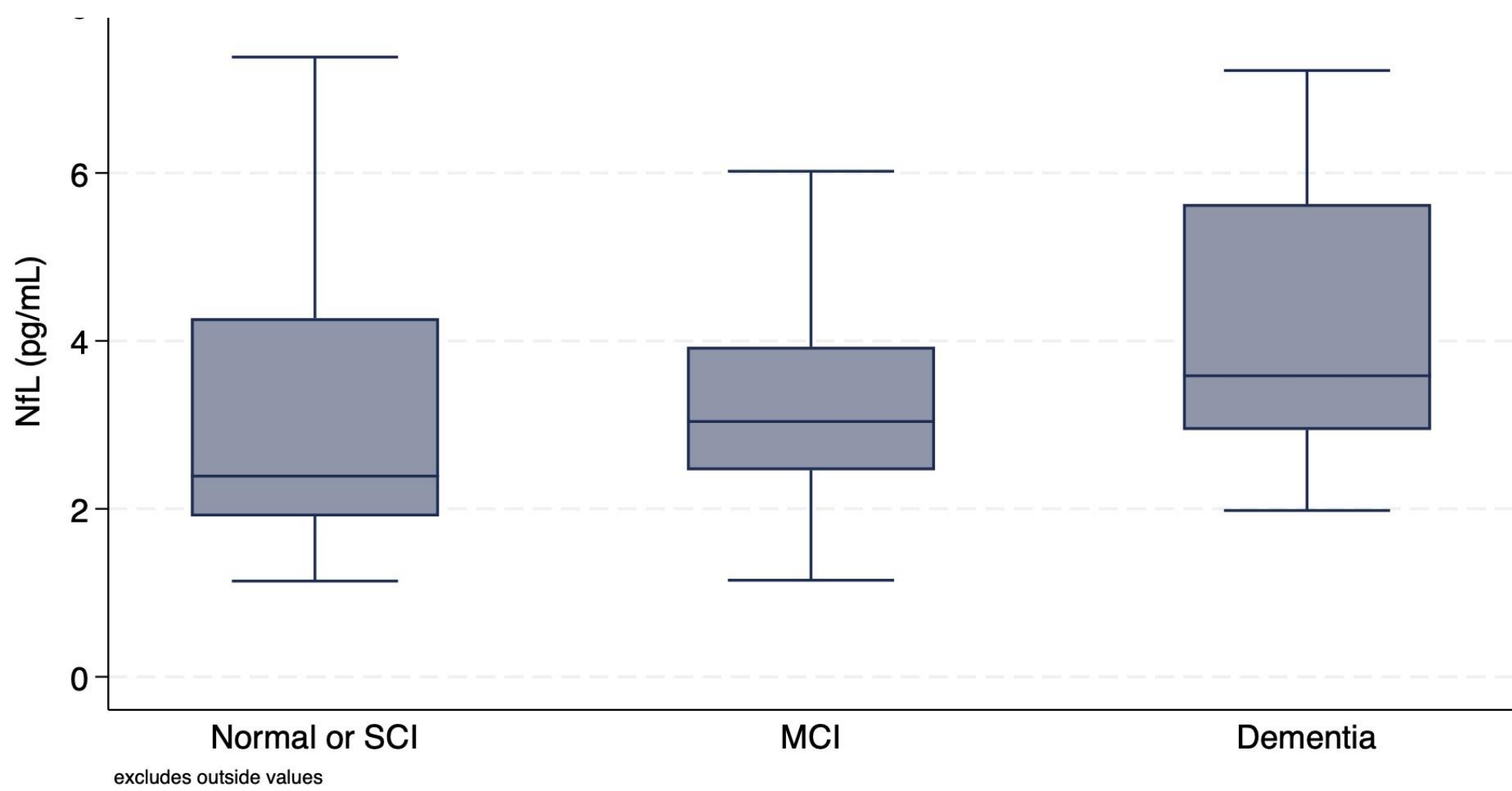
Table 1: Characteristics of the cohort

Characteristic	Overall Sample (n=82)
Age, mean (SD)	77.6 (8.1)
Sex, n(%) female	46 (56.1%)
Born overseas, n(%)	40 (48.8%)
Clinical Frailty Score, median (IQR)	4.5 (4-5)
Charlson Comorbidity Index, median (IQR)	5 (4-6)
MMSE, median (IQR) n=71	24 (19-28)
Geriatric Depression Scale, median (IQR) n=31	3 (1-4)
Days from initial assessment to diagnosis, median (IQR)	149 (84-200)

Table 2: Frequency of diagnoses

Diagnosis	Overall Sample (n=82) n (%)
Dementia	30 (37%)
AD dementia	22 (27%)
Non-AD dementia	8 (10%)
Mild cognitive impairment	34 (41%)
Non-amnesic	8 (10%)
Amnesic	26 (32%)
Subjective cognitive impairment/normal cognition	13 (16%)
Other	5 (6%)

Figure 1: Plasma neurofilament concentration by diagnostic groups



Area under ROC curve for NfL was 0.66 (95% CI 0.55-0.76). Using Youden’s index, a **cut-off NfL ≥2.69pg/mL** had sensitivity of 83.3% and specificity of 44.2%.

Figure 2: Plasma p-tau 217 concentration by diagnostic groups

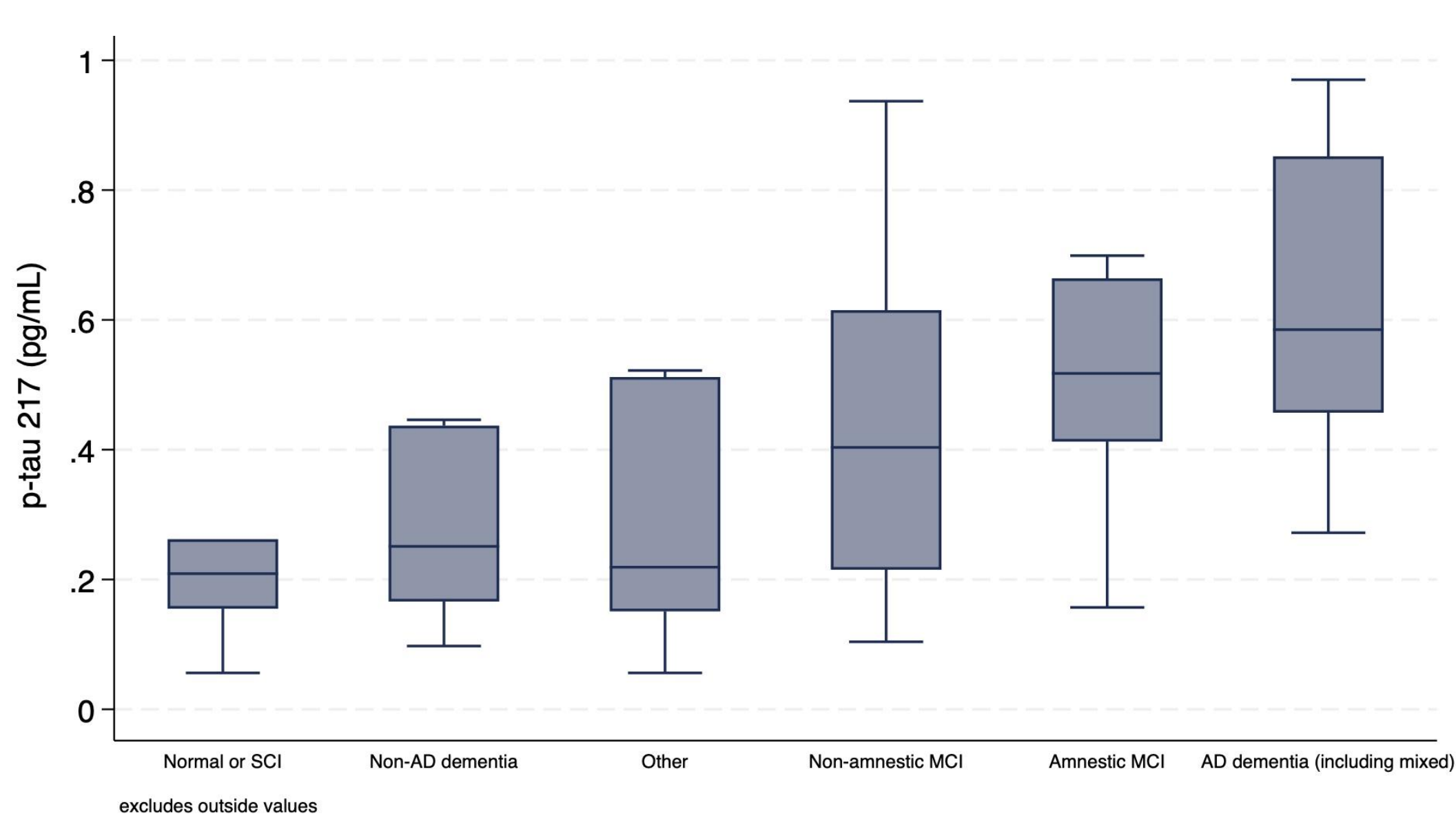
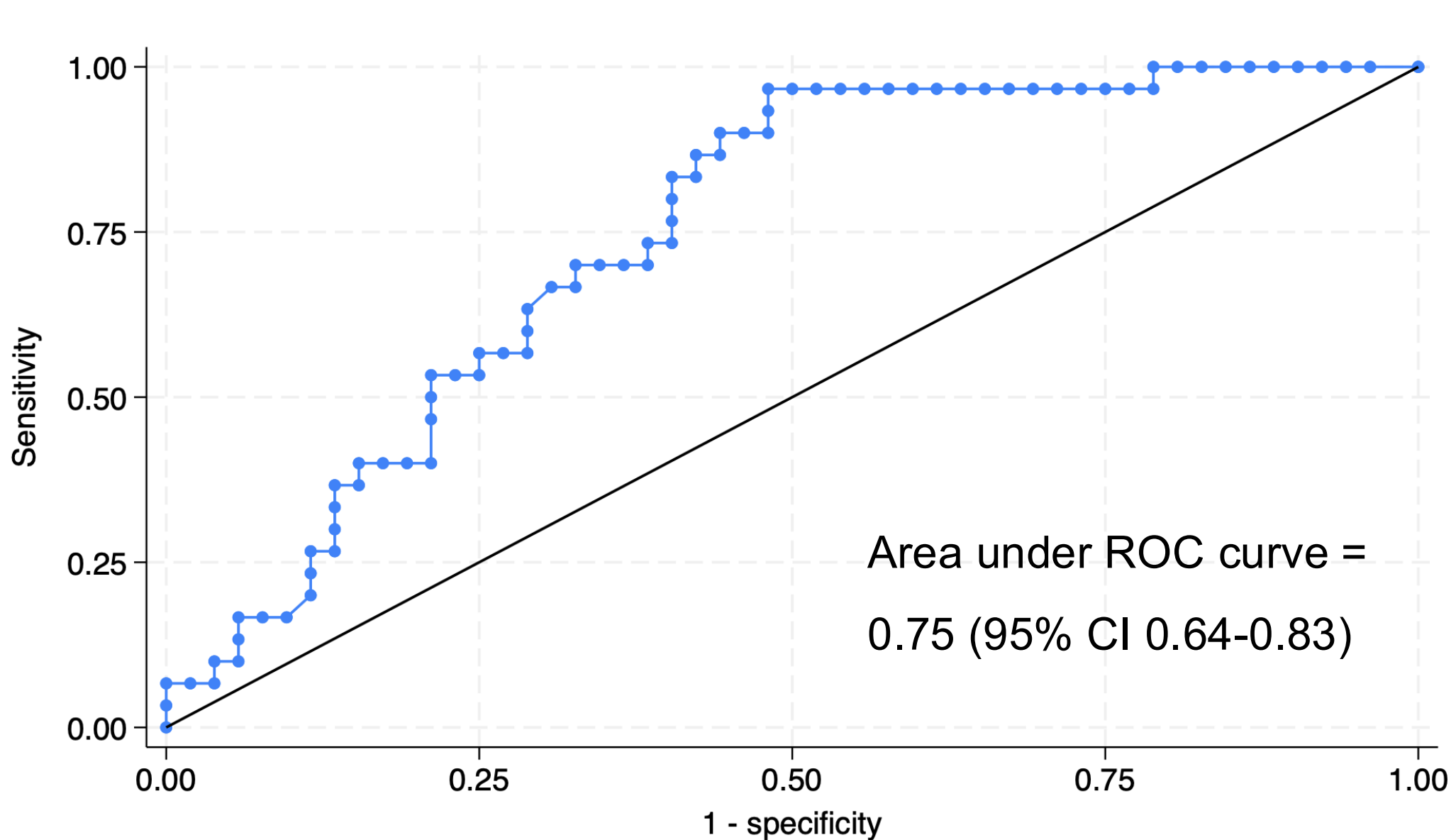


Figure 3: AUROC curve illustrating ability of p-tau 217 to classify participants into those with presumed amyloid-beta pathology (AD dementia and amnesic MCI) vs other



Using Youden’s index, a **cut-off p-tau 217 ≥0.27pg/mL** had sensitivity of 96.7% and specificity of 51.9%.

Conclusions

- This study demonstrates feasibility of pragmatic plasma biomarker studies within public hospital memory clinics
- NfL and p-tau 217 concentrations in the individual groups were consistent with their proposed utility
- Classification utility was mixed
 - Limited utility for NfL in the current study – potentially age effects, effects of other co-pathology
 - More promising classification utility for p-tau 217 – suggesting this might be helpful in predicting underlying AD pathology in this cohort