

# A Domestic Plasma P-tau217 Assay In China: Diagnostic Performance, Dual-pet Validation And Clinical Therapy Guidance

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## Background

- Independent validation of plasma p-tau217 assays against gold-standard PET is essential for clinical translation, yet diagnostic accuracy may vary across ethnicities. With rapid advances in anti-amyloid-beta (Aβ) therapies, China urgently needs population-specific blood biomarkers to streamline Alzheimer's disease (AD) diagnostic workflows.

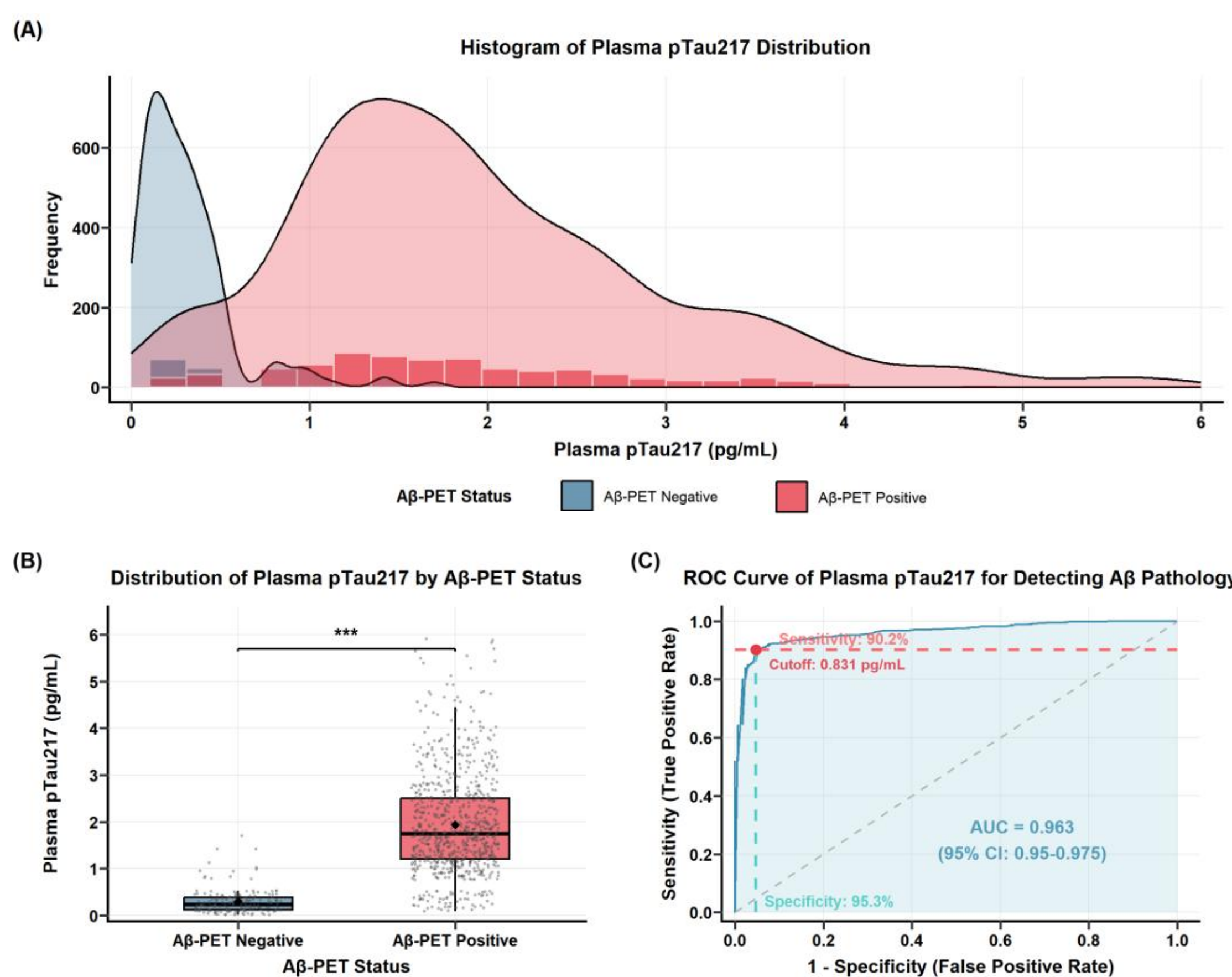
## Methods

- This study enrolled 1,026 real-world participants with Aβ-PET from multiple memory clinics, and 104 prospective participants with both Aβ-PET and tau-PET across 10 centers. Plasma p-tau217 was measured using a domestic Chinese single-molecule immunoassay platform. The diagnostic performance of a predefined dual-cutoff model (0.529/0.758 pg/mL) was evaluated against PET standards, and local optimization of the cutoffs was explored. We further explored APOE ε4 effects, correlations with other biomarkers (GFAP, NFL, Aβ42/Aβ40), and post-testing anti-Aβ treatment decisions.

## Results

- The predefined dual-cutoff model stratified patients into low-, intermediate-, and high-risk groups. In the real-world cohort, p-tau217 exhibited excellent accuracy in identifying Aβ-PET positive status (AUC=0.963, sensitivity 90.2%, specificity 95.3%) (Figure 1).

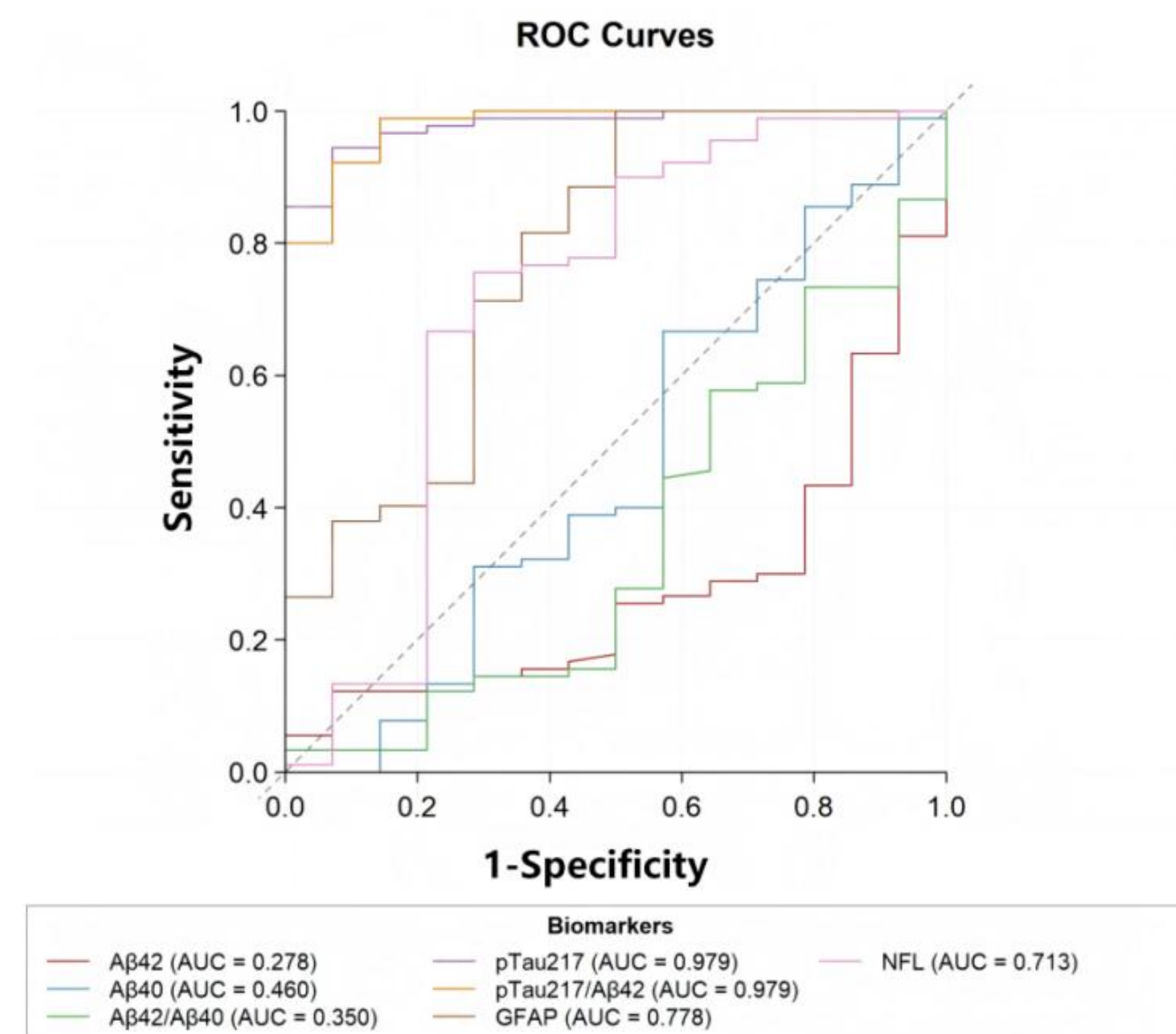
**Figure 1. Distribution of plasma pTau217 levels in Aβ-PET-positive and Aβ-PET-negative participants in the real-world cohort.**



Boxplots show median (center line), interquartile range (box), and range (whiskers). Individual data points are overlaid as jittered dots. The comparison between groups was performed using the Wilcoxon rank-sum test. \*\*\* $P < 0.001$ .

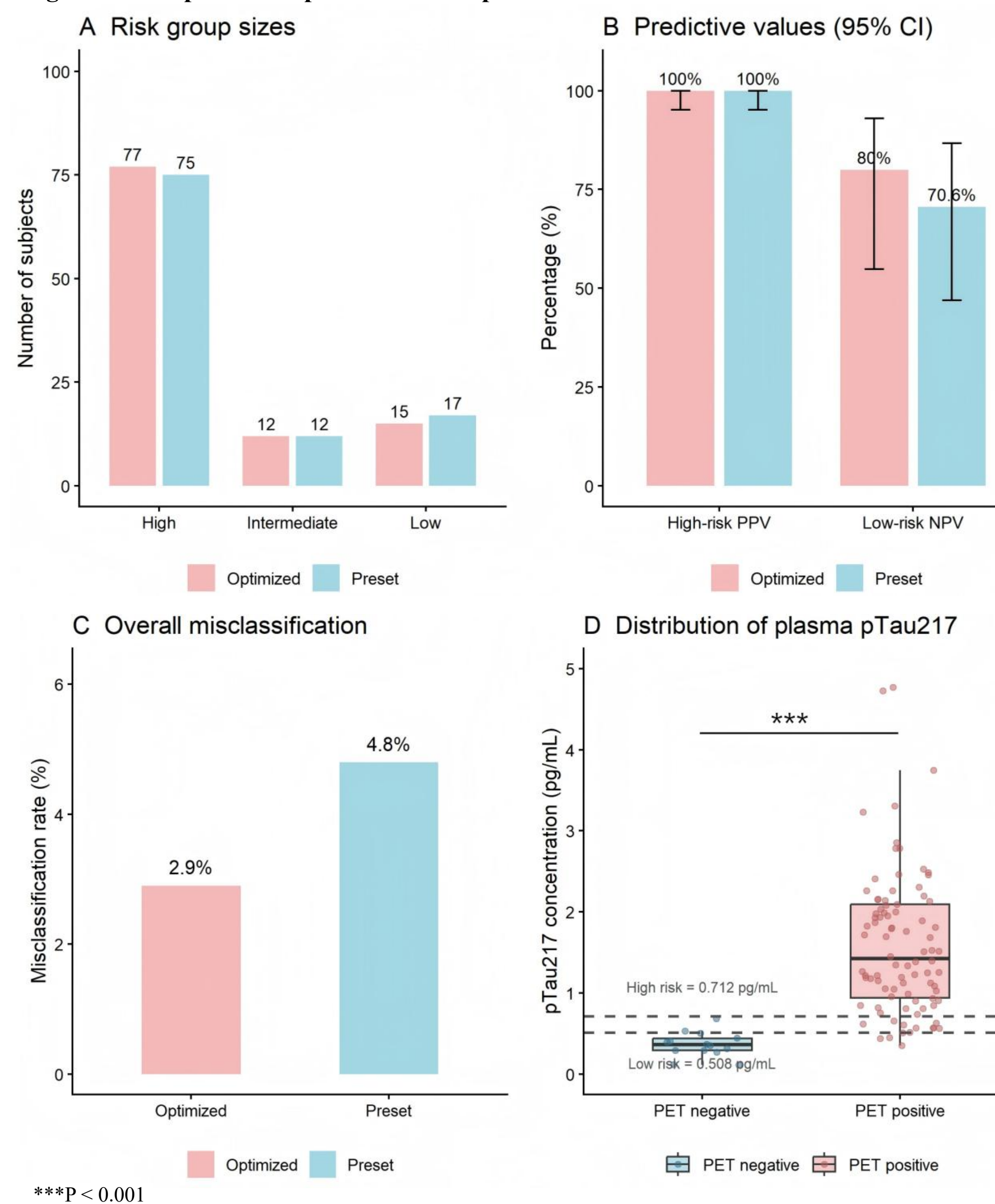
- In the prospective cohort, its AUC for diagnosing AD pathology (Aβ+ and Tau+) reached 0.979 (Figure 2).

**Figure 2. Receiver operating characteristic (ROC) curves of seven plasma biomarkers for discriminating PET-positive status**



- Using the dual-cutoff model as a pre-screening tool reduced the need for confirmatory amyloid PET scans by 85.6% (only 15/104 participants required PET: 12 intermediate-risk, 3 low-risk false-negatives). The predefined model achieved 100% positive predictive value (PPV) in the high-risk group, while local optimization of the cutoff values (0.508/0.712 pg/mL) improved the negative predictive value (NPV) of the low-risk group to 80% with a misclassification rate of 2.9% (Figure 3).

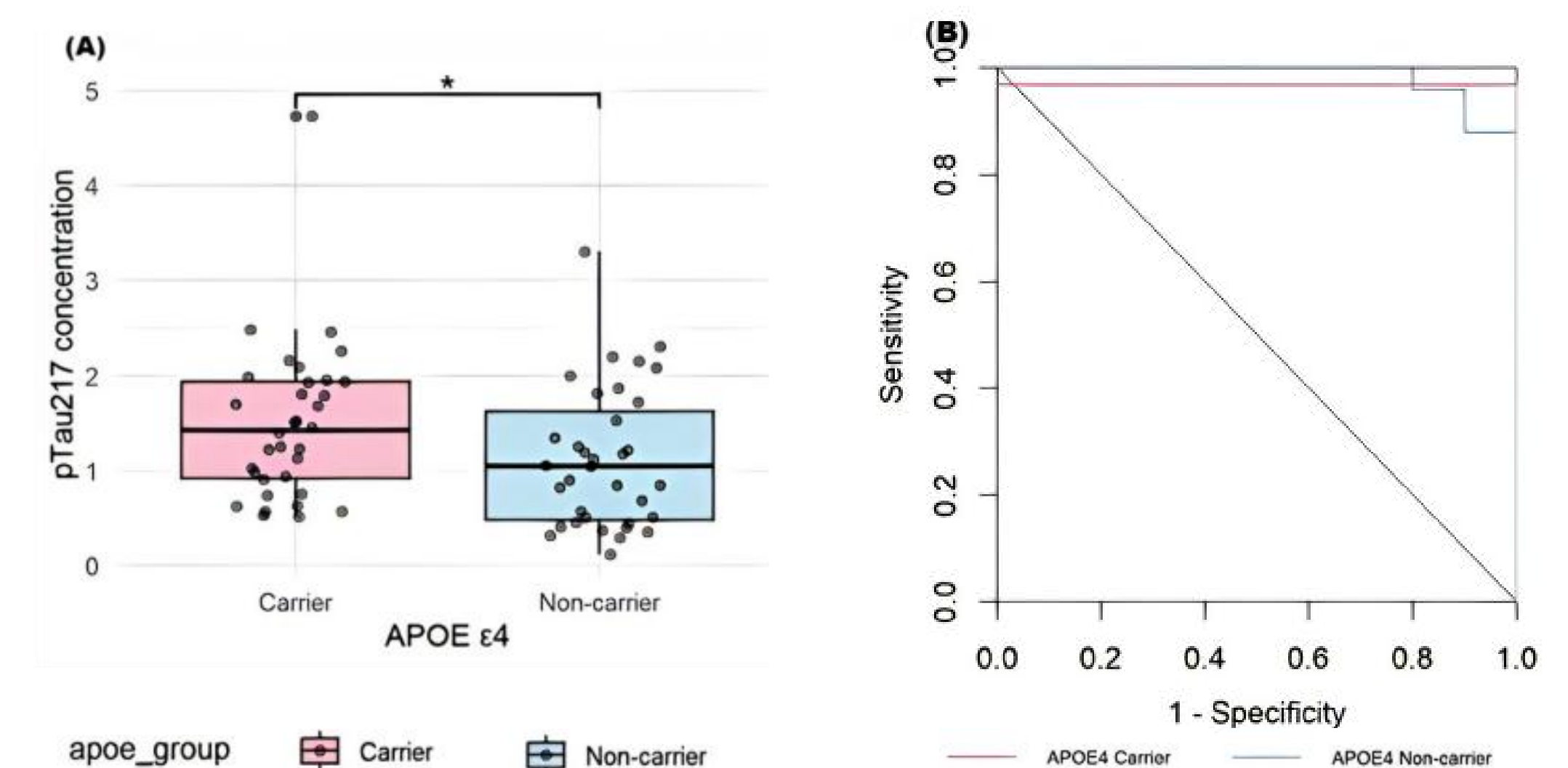
**Figure 3. Comparison of predefined vs. optimized dual-cutoff models for risk stratification**



\*\*\* $p < 0.001$

- APOE ε4 carriers exhibited higher p-tau217 levels ( $p=0.03$ ) with comparable diagnostic accuracy (Figure 4).

**Figure 4. Influence of APOE ε4 genotype on plasma pTau217 levels and diagnostic performance.**



(A) Distribution of plasma pTau217 levels in APOE ε4 carriers vs. non-carriers \* $P=0.03$ . (B) ROC curves of pTau217 for predicting PET positivity stratified by APOE ε4 carrier status.

- Plasma p-tau217 was significantly correlated with MMSE scores ( $p=-0.43$ ,  $p<0.001$ ), and in PET-positive populations, it was positively correlated with GFAP ( $r=0.245$ ,  $p=0.022$ ) and NFL ( $r=0.380$ ,  $p<0.001$ ) (Table 1).

**Table 1. Correlation of plasma pTau217 with other biomarkers**

| Variable             | Group   | r            | P            | 95% CI                 |
|----------------------|---------|--------------|--------------|------------------------|
| pTau217 vs Aβ1_40    | PET (+) | 0.142710151  | 0.179653833  | 0.143 (-0.066, 0.340)  |
|                      | PET (-) | 0.125274725  | 0.669582397  | 0.125 (-0.434, 0.615)  |
|                      | Overall | 0.093065684  | 0.347393038  | 0.093 (-0.101, 0.281)  |
| pTau217 vs Aβ1_42    | PET (+) | 0.182559771  | 0.08503157   | 0.183 (-0.025, 0.375)  |
|                      | PET (-) | -0.094505495 | 0.747938261  | -0.095 (-0.595, 0.459) |
|                      | Overall | -0.004529014 | 0.963605901  | -0.005 (-0.197, 0.188) |
| pTau217 vs Aβ42_Aβ40 | PET (+) | 0.109225159  | 0.305464065  | 0.109 (-0.100, 0.309)  |
|                      | PET (-) | -0.336263736 | 0.239792202  | -0.336 (-0.736, 0.237) |
|                      | Overall | -0.034119734 | 0.730959797  | -0.034 (-0.225, 0.160) |
| pTau217 vs GFAP      | PET (+) | 0.244608578  | 0.022409046* | 0.245 (0.036, 0.433)   |
|                      | PET (-) | -0.068131868 | 0.81698388   | -0.068 (-0.578, 0.480) |
|                      | Overall | 0.362641491  | <0.001***    | 0.363 (0.180, 0.521)   |
| pTau217 vs NFL       | PET (+) | 0.379693392  | <0.001***    | 0.380 (0.186, 0.545)   |
|                      | PET (-) | 0.314285714  | 0.273804903  | 0.314 (-0.260, 0.724)  |
|                      | Overall | 0.426505879  | <0.001***    | 0.427 (0.254, 0.573)   |

Legend: Data are expressed as Spearman correlation coefficients  $r$  with 95% confidence intervals (CI) and  $p$ -values. The population consists of all subjects with valid PET results. Confidence intervals are approximated using Fisher's  $z$  transformation.

Abbreviations: Aβ, amyloid-beta; GFAP, glial fibrillary acidic protein; NFL, neurofilament light chain; PET, positron emission tomography; PET (+), PET positive (indicating amyloid pathology); PET (-), PET negative; CI, confidence interval.

Significance levels: \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ .

- Notably, 51.2% of patients initiated anti-Aβ therapy following p-tau217 testing.

## Conclusion

- The domestic Chinese plasma p-tau217 assay demonstrates diagnostic performance comparable to international standards in both real-world and prospective Chinese cohorts. Applying the optimized dual-cutoff model effectively stratifies patient risk, reducing the number of amyloid PET scans without compromising diagnostic accuracy, and the subsequent anti-Aβ therapy initiation rate is high. Therefore, plasma p-tau217 testing can directly inform and accelerate precision treatment decisions for AD.