

Cognitive Stage–Adapted Amyloid PET Thresholds for Plasma p-tau217 Testing

Min Young Chun^{1,2†}, Young Ju Kim^{3†}, Heekyoung Kang^{4†}, Tobias Bittner⁵, Gwendlyn Kollmorgen⁶, Annunziata Di Domenico⁷, Henrik Zetterberg⁸, Fernando Gonzalez-Ortiz⁸, Nicholas J Ashton⁸, Michael W. Weiner⁹, Joel Braunstein¹⁰, Philip Verghese¹⁰, Tim West¹⁰, Matthew R. Meyer¹⁰, Shin-Cheng Tzeng¹⁰, Jihwan Yun¹¹, Hyemin Jang¹², Hee Jin Kim^{3,4}, Duk L. Na¹³, Jun Pyo Kim^{3,4}, and Sang Won Seo^{3,4} on behalf of the ADNI, and the K-ROAD studies

¹Department of Neurology, Yonsei University College of Medicine, Seoul, South Korea; ²Department of Neurology, Yonsei Severance Hospital, Yonsei University Health System, Yonjin, South Korea; ³Alzheimer's Disease Convergence Research Center, Samsung Medical Center, Seoul, Korea; ⁴Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; ⁵F. Hoffmann–La Roche AG, Switzerland; ⁶Roche Diagnostics GmbH, Germany; ⁷Roche Diagnostics International Ltd, Switzerland; ⁸Department of Psychiatry and Neurochemistry, University of Gothenburg, Sweden; ⁹Department of Radiology and Biomedical Imaging, University of California, USA; ¹⁰C2N Diagnostics, LLC, USA; ¹¹Department of Neurology, Kyung Hee University Medical Center, South Korea; ¹²Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, South Korea; ¹³Happymind Clinic, South Korea

- **Optimal amyloid PET CL thresholds for plasma p-tau217 testing differed by cognitive stage: 20 CL in CI and 25–30 CL in CU.**
- **Adding Aβ42/40 provided limited incremental value in CI but modest benefit in CU.**
- **Double-cutoff strategies offered limited added value in high-performing assays because of cutoff inversion.**

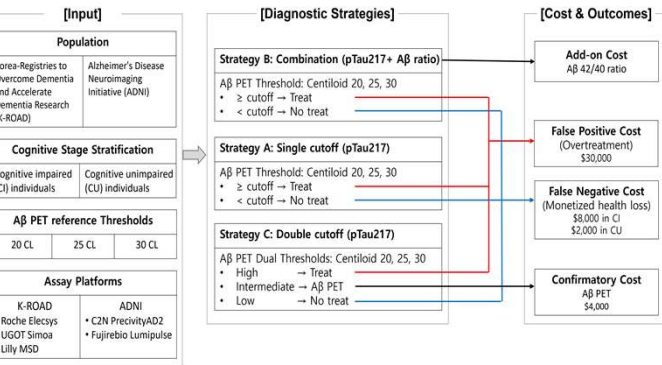


Poster Number: Sunday-1042
aaic2026.8a41008

INTRODUCTION

- Plasma p-tau217 is a promising prescreening tool for Aβ pathology before confirmatory amyloid PET.
- Centiloid (CL) thresholds of 20–30 are commonly used to define Aβ PET positivity, but the optimal threshold may differ by cognitive stage.
- Whether the choice of CL reference standard affects plasma biomarker diagnostic performance in cognitively impaired (CI) vs. cognitively unimpaired (CU) individuals remains unclear.
- **Objective:** 1) To determine whether the optimal amyloid PET CL threshold for plasma p-tau217 testing differs by cognitive stage.
2) To compare the diagnostic and economic performance of single-cutoff, double-cutoff, and combination strategies.

METHODS

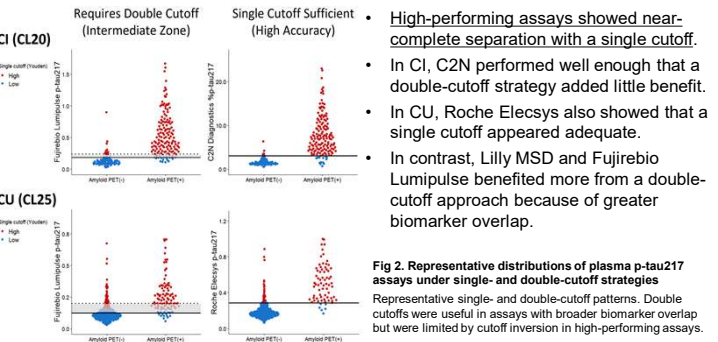


- **Population:** 2,359 participants with plasma sampling & Aβ PET within 1 year
- **K-ROAD:** n=1,679 (411 CU, 1,268 CI); **NA-ADNI:** n=680 (442 CU, 238 CI)
- Plasma p-tau217 performance was evaluated against Aβ PET positivity using CL 20, 25, and 30 thresholds.
- Assays included Roche Elecsys, UGOT Simoa, Lilly MSD, C2N Diagnostics, and Fujirebio Lumipulse.
- 3 diagnostic strategies were compared: **single cutoff, double cutoff, and p-tau217 + Aβ42/40 combination.**
- **Analyses:** ROC/AUC across PET thresholds (20/25/30 CL), p-tau217 alone vs p-tau217 + Aβ42/40, and prespecified double cutoffs.

RESULTS

Table. Demographic and clinical characteristics of participants					
Characteristics	K-ROAD cohort (n=1,679)			NA-ADNI cohort (n=680)	
	CU (n=411)	CI (n=1,268)	P value	CU (n=442)	CI (n=238)
Age, mean (SD), years	69.2 (8.4)	72.6 (8.4)	<.001	72.0 (8.6)	74.7 (8.3)
Female, n (%)	271 (65.9)	801 (63.2)	.310	285 (64.5)	122 (51.3)
Education, mean (SD)	11.1 (4.7)	10.1 (4.7)	<.001	16.6 (2.5)	16.1 (2.7)
MMSE, score	27.8 (2.2)	23.6 (4.6)	<.001	28.9 (1.3)	26.4 (3.3)
APOE ε4 carrier, n (%)	93 (22.6)	521 (41.2)	<.001	129 (31.9)	105 (47.9)
Aβ PET positivity, n (%)	79 (19.2) / 70 (17.0) / 59 (14.4)	695 (54.8) / 676 (53.3) / 649 (51.2)	<.001	109 (24.7) / 100 (22.6) / 90 (20.4)	146 (61.3) / 136 (57.1) / 132 (55.5)
Threshold: CL 20/ 25/ 30					
Diagnosis (MCI/Dementia), n (%)		975 (76.9) / 293 (23.1)		186 (78.2) / 52 (21.8)	

Representative Single vs Double Cutoff Patterns



Incremental Value of Adding Aβ42/40

- Adding the plasma Aβ42/40 ratio to p-tau217 provided minimal benefit in CI (DeLong P 0.174–0.998), as baseline discrimination was already high.
- In CU, the combined model showed modest improvement, most pronounced at 20 CL. C2N Diagnostics remained significant across all thresholds, whereas Lilly MSD lost significance at 30 CL.

CONCLUSIONS

- **Optimal Aβ PET CL thresholds for plasma p-tau217 differ by cognitive stage.**
- **Lower threshold (20 CL) maximizes sensitivity in CI; Higher thresholds (25–30 CL) improve specificity in CU.**
- **For high-precision assays, a single cutoff is sufficient; double cutoffs add little.**
- **Findings support stage-adapted, assay-specific blood-based triage in the era of disease-modifying therapies.**

Diagnostic Performance Across Thresholds

- In CI, diagnostic performance peaked at **CL 20**.
 - In CI, AUC ranged from 0.923 to 0.962, indicating consistently high performance.
 - In CU, performance was more assay-dependent and improved at **CL 25–30**.
 - In CU, AUC ranged from 0.841 to 0.953
- **Lower PET thresholds favored sensitivity in CI, whereas higher thresholds improved specificity in CU.**

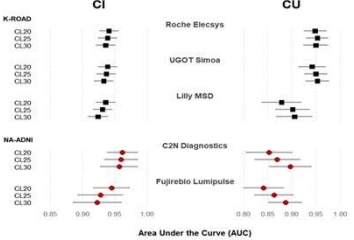


Fig 1. Diagnostic performance of plasma p-tau217 across platforms and cutoff strategies. AUC for p-tau217 for detecting Aβ PET positivity at CL thresholds of 20, 25, and 30, stratified by cognitive status (CI and CU) and assay platform

Exploratory Cost Patterns

- In CI, CL 20 was associated with the lowest per-person cost.
- In CI, lower thresholds maximize sensitivity and reduce cost.
- In CU, higher thresholds improve specificity and reduce false positives.

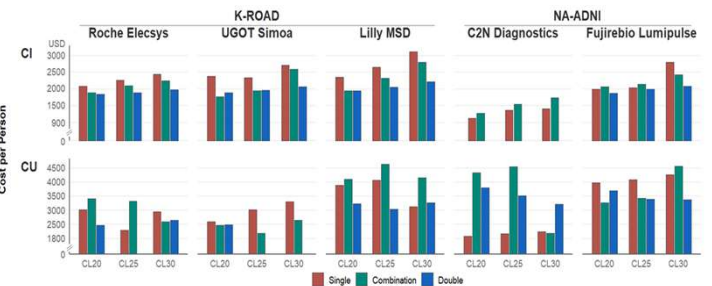


Fig 3. Cost comparison across diagnostic strategies by assay platforms, cognitive status, and CL threshold. Bars represent exploratory per-person costs incorporating three downstream cost components: false-positive misclassification (\$30,000 per person for unnecessary anti-Aβ therapy), false-negative misclassification (\$8,000 per person in CI and \$2,000 per person in CU), and confirmatory Aβ PET for intermediate cases (\$4,000 per scan). Plasma assay costs were not included.

CONTACT

Min Young Chun, myc5198@gmail.com
Sang Won Seo, sangwonseo@empas.com