

Multi-platform Evaluation of Plasma p-tau217 Double Cutoff Strategies for Cost-Effective Triage of Tau PET Positivity



Heekyoung Kang^{1†}, Yuna Gu^{1†}, Jungah Lee¹, Soyeon Yoon¹, Henrik Zetterberg², Kaj Blennow², Fernando Gonzalez-Ortiz², Nicholas J. Ashton², Theresa A. Day³, Michael W. Weiner⁴, Daeun Shin¹, Sohyun Yim¹, Seonghyeon Kim¹, Hee Kyung Park¹, Min Young Chun¹, Eun Hye Lee¹, Jun Pyo Kim¹, Hee Jin Kim¹, Duk L. Na¹, Hyemin Jang¹, Sang Won Seo^{1*}

¹Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
²Institute of Neuroscience and Physiology, University of Gothenburg & Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Gothenburg, Sweden
³Eli Lilly and Company, Indianapolis, IN, USA
⁴Department of Radiology and Biomedical Imaging, University of California, San Francisco, CA, USA



Plasma p-tau217 predicts tau PET positivity across platforms, while double cutoff strategies support more cost-effective tau PET triage by reducing misclassification and routing uncertain cases to confirmatory PET

INTRODUCTION



- Tau PET is the reference standard for tau stratification, but it is costly and limited in access.
- Plasma p-tau217 reflects amyloid and tau pathology, yet a single cutoff can misclassify tau PET status.
- We compared single- and double-cutoff strategies across assay platforms in a tau-enriched cohort and a tau-scarce cohort, and evaluated their cost implications.

METHODS

K-ROAD
(Tau-enriched)
N = 120



- Tau PET+ 61.7%
- Aβ+ 83.3%
- Mean age 72.1
- APOE ε4 54.2%

NA-ADNI
(Tau-scarce)
N = 280



- Tau PET+ 20.4%
- Aβ+ 48.6%
- Mean age 76.6
- APOE ε4 33.2%

1. Cutoff strategy

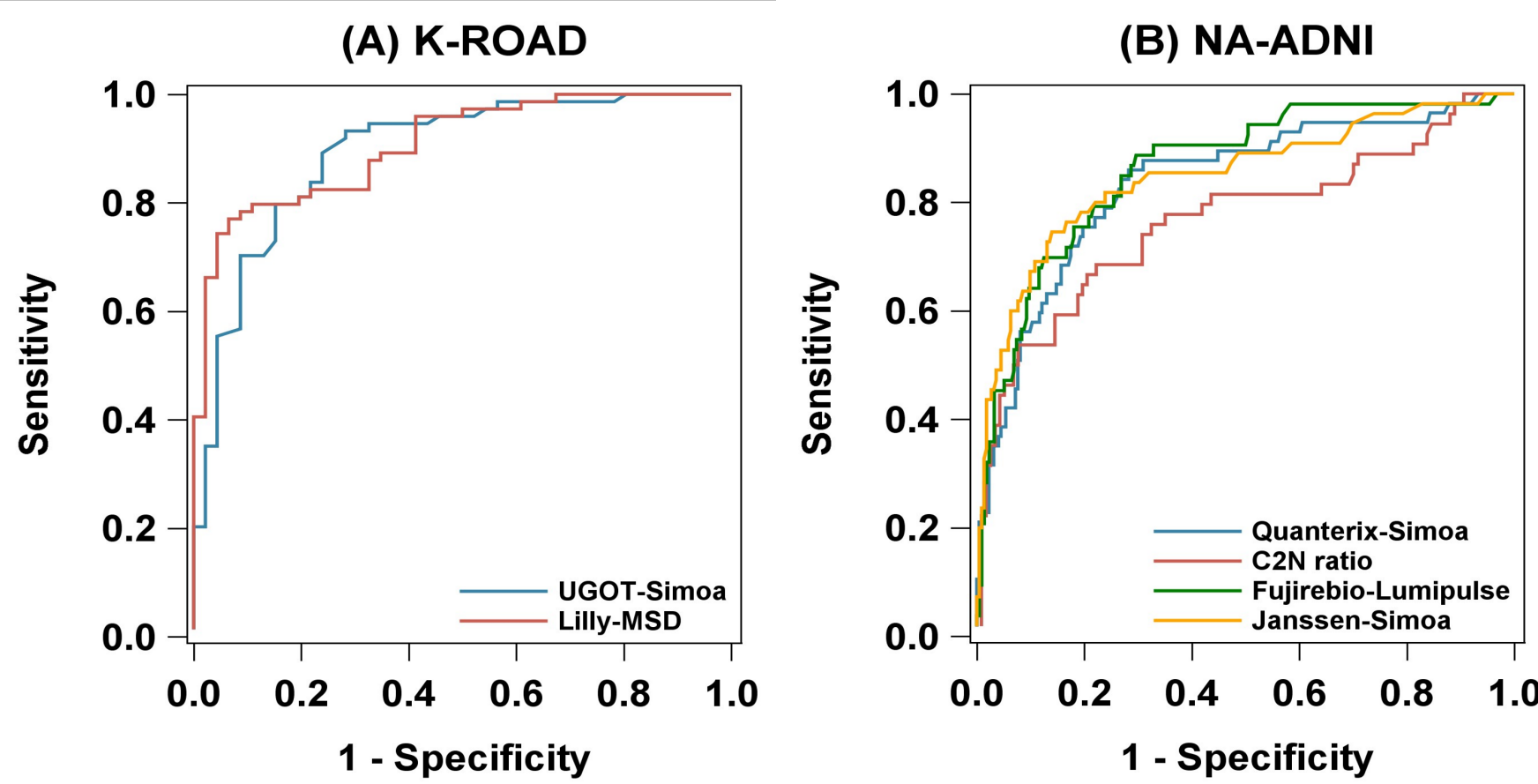
- **Single cutoff:**
One optimal threshold by Youden's index
Low risk | High risk
- **Double cutoff:**
Lower threshold at 90% sensitivity
Upper threshold at 90% specificity
Low risk | Intermediate | High risk

2. Cost model

- Confirmatory tau PET: \$4,000
- False positive: unnecessary tau-targeted therapy, \$30,000
- False negative: missed clinical benefit, \$8,000

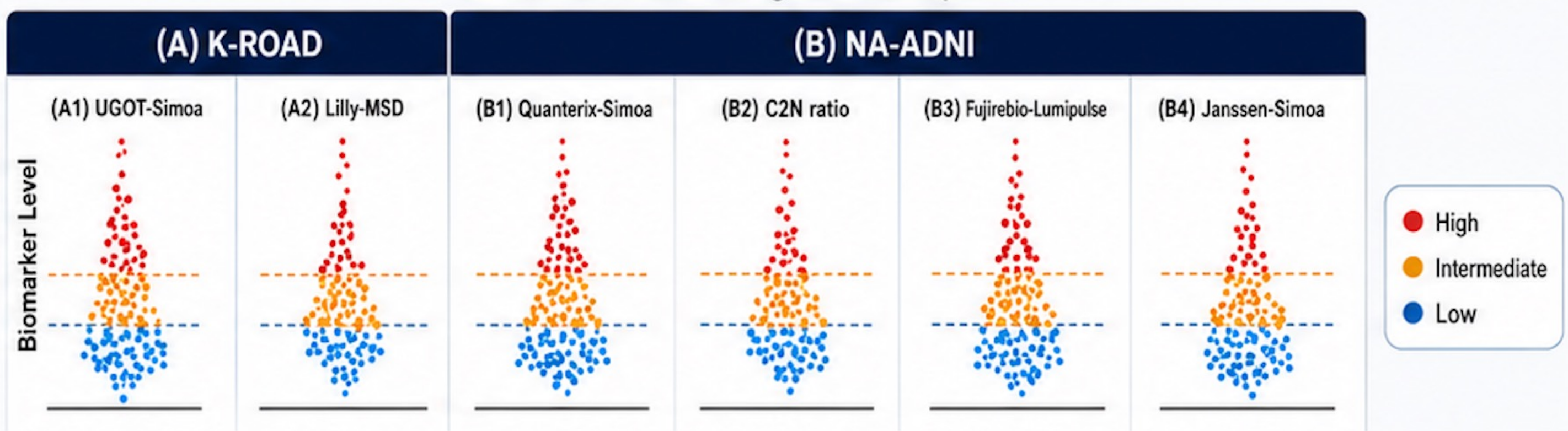
RESULTS

1. Single Cutoff Performance: ROC Curves for Tau PET Prediction



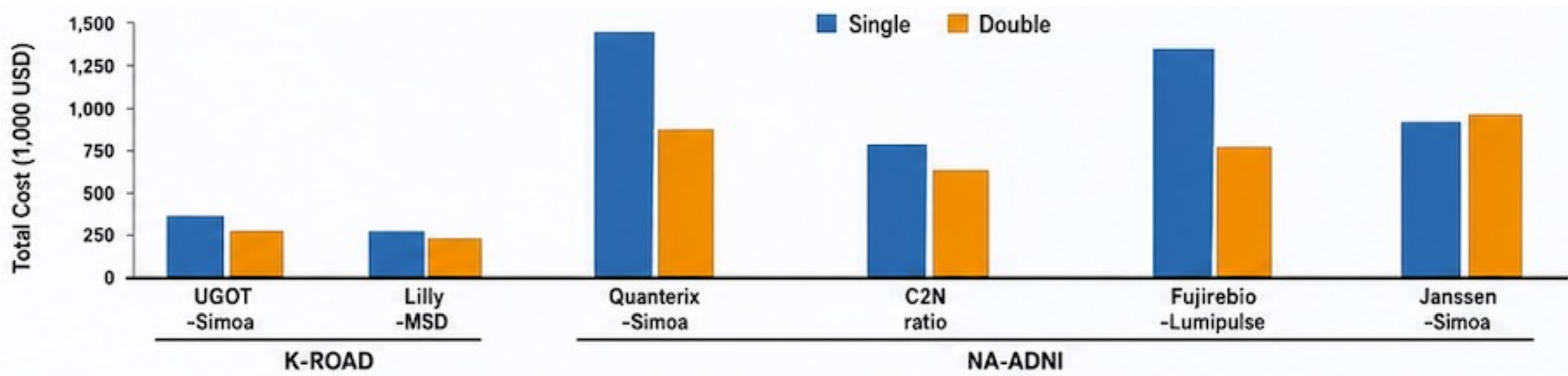
✓ Good discrimination across most platforms (AUC range: 0.767–0.907)

2. Double Cutoff Classification: Low / Intermediate / High Groups



✓ Double cutoffs prioritise tau PET for uncertain cases.

3. Cost Comparison: Single vs. Double Cutoff Strategies



CONCLUSION



Plasma p-tau217 predicted tau PET positivity with good accuracy across most assay platforms.



Double cutoff strategies improved classification modestly, but their clinical value depended on cohort tau prevalence and assay platform.



The greatest practical value lies in reducing misclassification related costs and guiding confirmatory tau PET use, rather than replacing tau PET universally.

Cost assumptions

- Confirmatory tau PET: \$4,000
- False positive: \$30,000
- False negative: \$8,000



The double-cutoff strategy reduced total cost in most settings, with effects varying by cohort tau prevalence and assay platform.