

# Alzheimer's Disease

## Blood-based multibiomarker models

**?** Can using multiple plasma biomarkers help evaluate for amyloid pathology among patients with mild cognitive impairment (MCI) or suspected Alzheimer's disease (AD)?

### Background

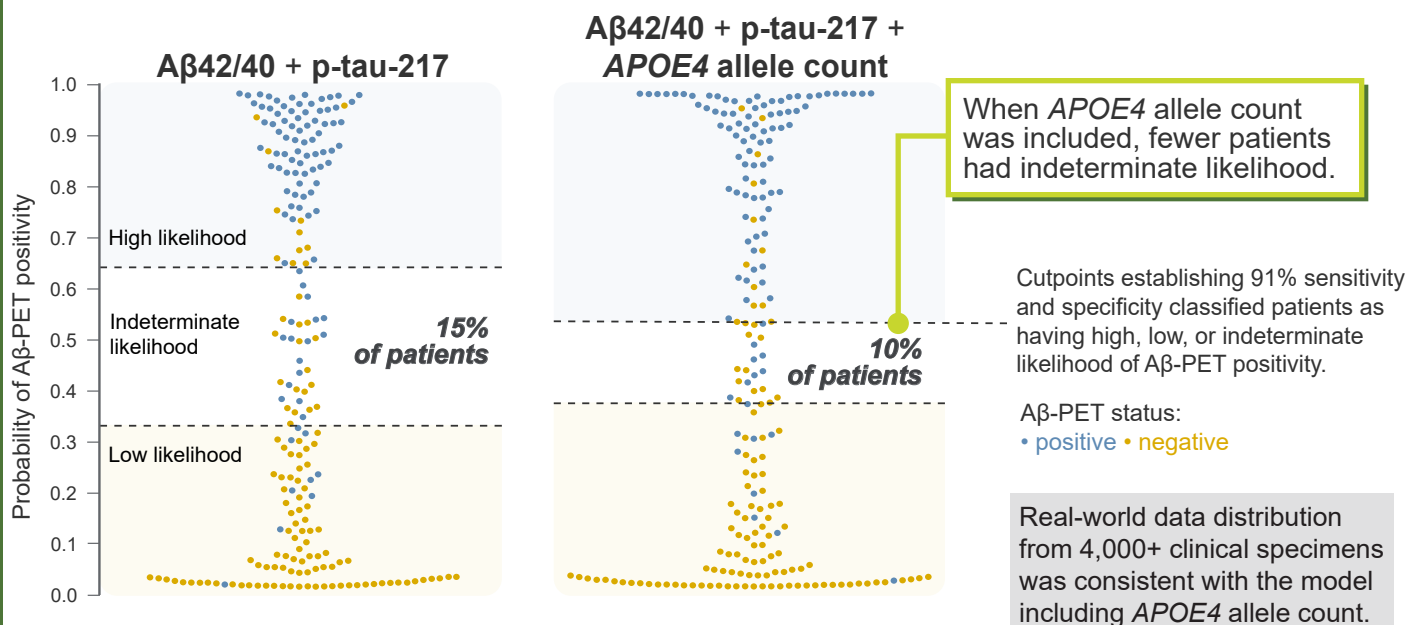
Current therapies for MCI and mild AD require correct diagnosis, but traditional methods of identifying AD pathology (PET imaging, CSF evaluation) can be costly or invasive. Blood biomarkers offer a scalable alternative, though they should meet performance requirements when set at  $\geq 90\%$  sensitivity and specificity in the intended-use population (MCI and AD).<sup>1</sup>

### Methods and Results

Plasma specimens from 215 participants with MCI or AD were analyzed for A $\beta$ 42/40 ratio, p-tau217 levels, and apolipoprotein  $\epsilon$ 4 (*APOE4*) allele count. Participants were assessed for PET status; the PET-negative and PET-positive cohorts were matched for demographics. Biomarker combinations were evaluated.

## Clinical performance of biomarker combinations<sup>2</sup>

**Both models predicted A $\beta$ -PET status with acceptable performance for clinical use<sup>a</sup>**  
Sensitivity and specificity, 91%; accuracy, 85%-87%; positive and negative predictive values,<sup>a</sup> 90%



A $\beta$ , beta-amyloid; CI, confidence interval; PET, positron emission tomography; ptau, phosphorylated tau.

<sup>a</sup> According to recommendations from the Global CEO Initiative on Alzheimer's Disease for 50% prevalence of amyloid positivity.<sup>1</sup>

**→** Among individuals with MCI or suspected AD, likelihood of amyloid pathology can be assessed with multiple plasma biomarkers via a 2-cutpoint approach. Using A $\beta$ 42/40 and p-tau217 offers an accurate approach, while incorporating *APOE4* allele count enhances performance.

1. Schindler SE, Galasko D, Pereira AC, et al. Acceptable performance of blood biomarker 502 tests of amyloid pathology - recommendations from the Global CEO Initiative on 503 Alzheimer's Disease. *Nat Rev Neurol*. 2024;20:426-439.
2. Weber DM, Stroh MA, Taylor SW, et al. Development and clinical validation of blood-based multibiomarker models for the evaluation of brain amyloid pathology. *Neurol Clin Practice*. 2025;15:e200546. doi:10.1212/CPJ.00000000002

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