THE ROLE OF BLOOD BIOMARKERS IN

Alzheimer's Disease Diagnosis

Clinical Context and Unmet Need

Alzheimer's disease (AD) is the leading cause of dementia worldwide, accounting for **60%-80% of cases.**[1]

AD pathophysiology includes **β-amyloid plaques and tau NFTs** that begin accumulating decades before symptoms emerge.

Disease-modifying therapies (DMTs) are currently indicated for symptomatic individuals with biomarker-confirmed amyloid pathology.[1]

Traditional modalities for confirming amyloid pathology include amyloid PET imaging and CSF testing. Each has unique benefits and limitations regarding accessibility and invasiveness.[1]

Blood biomarkers (BBMs) are emerging as an additional tool for confirming amyloid pathology in symptomatic individuals. Their use should be guided by clinical context and current guidelines and recommendations.[1,2]

Who Is Eligible for BBM Testing?

Clinical guidelines and recommendations for the use of BBMs, including those from the Alzheimer's Association (guidelines) and the BBM Workgroup of the Global CEO Initiative (recommendations), suggest that BBM testing may be considered for individuals with objective evidence of cognitive impairment and/or a history of progressive cognitive decline, following a comprehensive assessment to evaluate for other potential medical causes. Decisions regarding BBM testing should be individualized and based on clinical judgment.[1,2]

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Performance Standards for Confirmatory BBM Use[1]

Performance standards for BBM tests, as recommended by the Global CEO Initiative on Alzheimer's Disease, include sensitivity and specificity thresholds (e.g., ≥90%). Refer to Schindler SE, et al. for detailed recommendations.

Sensitivity ≥90%:

- Correctly identifies at least 9/10 people with amyloid pathology

Specificity ≥90%:

- Correctly excludes at least 9/10 people without pathology

Intermediate Results <15-20%:

- Using two cut-offs should yield intermediate results in <15-20% of tested individuals, as higher rates may hinder diagnostic clarity

Why Predictive Values Matter for BBMs[1]

Positive and negative predictive values reflect the likelihood that BBM results truly reflect the presence or absence of amyloid pathology. Their values depend on the prevalence of amyloid pathology in the tested population (see Schindler SE, et al.).

Based on current guidelines and recommendations, BBMs that meet confirmatory standards may be integrated into secondary care for individuals with cognitive symptoms.[1,2]

- **DMT eligibility (which may include *APOE* ε4 genotyping)**[1,2]
- **Care planning**[1,2]

BBMs are validated for symptomatic individuals only, not for preclinical/asymptomatic use.

Abbreviations: AD=Alzheimer's Disease; APOE=Apolipoprotein E; BBM=Blood Biomarker; CSF=Cerebrospinal Fluid; DMT=Disease Modifying Therapy; NFTs=Neurofibrillary Tangles; PET=Positron Emission Tomography.

References: 1. Schindler SE, et al. *Nat Rev Neurol.* 2024;20(7):426-439. 2. Palmqvist S, et al. *Alzheimers Dement.* 2025;21(7):e70535.

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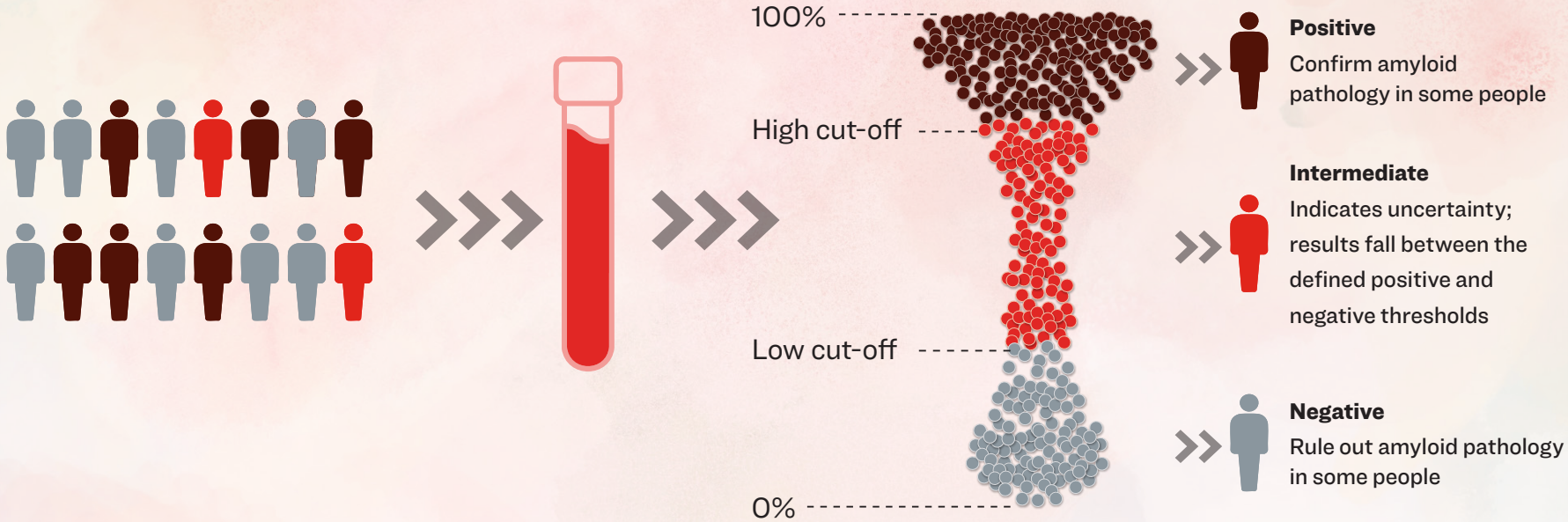
The two-threshold strategy may help guide next clinical steps

People with cognitive symptoms	Blood-based biomarker testing	Probability of amyloid PET positivity	Results



As BBMs become more widely available, healthcare systems may need to address barriers to care, such as insurance coverage and education gaps among patients, caregivers, and care providers.

BBMs are validated for symptomatic individuals only, not for preclinical/asymptomatic use.

BBM=Blood Biomarker; PET=Positron Emission Tomography.

Reference: Schindler SE, et al. *Nat Rev Neurol.* 2024;20(7):426-439. Two-threshold strategy figure adapted from Schindler SE, et al. *Nat Rev Neurol.* 2024;20(7):426-439 [Fig. 2].

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