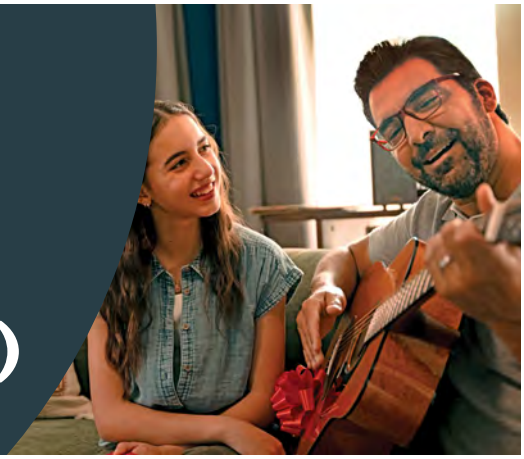
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Clinical Use and Interpretation of BLOOD BIOMARKERS IN ALZHEIMER'S DISEASE (AD)



Symptom-based diagnosis leaves AD detected late, missed, or misclassified[1]

DIAGNOSED TOO LATE	Globally, AD diagnosis is delayed an average of 3.6 years after symptom onset[2]
UNDERDIAGNOSED	An estimated 75% of people with dementia worldwide are undiagnosed[3,4]
MISDIAGNOSED	Autopsy and biomarker studies have previously found that 13-30% of individuals clinically diagnosed with Alzheimer's dementia did not have AD-related brain pathology[3,5]

This finding may stem from the historical reliance on symptom-based diagnosis; recently, the field has been moving toward a more biologically driven definition that focuses on the AD pathological hallmarks of amyloid and tau[6,7]

Who is eligible for blood biomarker testing?

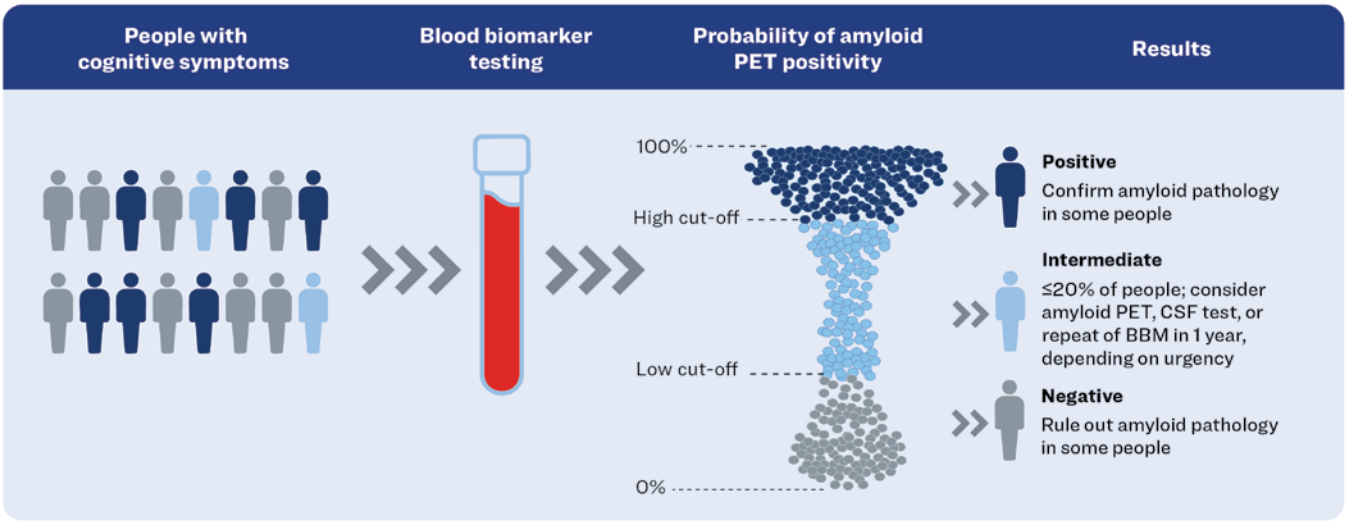
Clinical guidelines and recommendations for the use of blood biomarker tests, including those from the Alzheimer's Association (guidelines) and the Global CEO Initiative (CEOi) Blood-Based Biomarker Workgroup* (recommendations), suggest that blood biomarker testing may be considered for individuals with 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 blood biomarker testing should be individualized and based on clinical judgment.[8,9]

Consider performance standards when selecting blood biomarker tests[8-10]

- Blood tests offer an affordable and accessible alternative to existing tools, but performance still varies, highlighting the need for clear clinical standards
- To address this challenge, the Global CEOi Blood-Based Biomarker Workgroup has published recommendations for AD blood biomarker tests in clinical use
  - Blood biomarker tests can be used to confirm disease pathology without further PET or CSF testing
  - Confirmatory tools should meet the following criteria:
    - Blood biomarker (Confirmatory): ≥90% Sensitivity / ≥90% Specificity (single cut-point)
    - Blood biomarker (Confirmatory): ≥90% Sensitivity / ≥90% Specificity / ≤20% Intermediate results (dual cut-point)

Interpreting blood biomarker test results

The use of a dual cut-point approach leads to three categories of results[9]



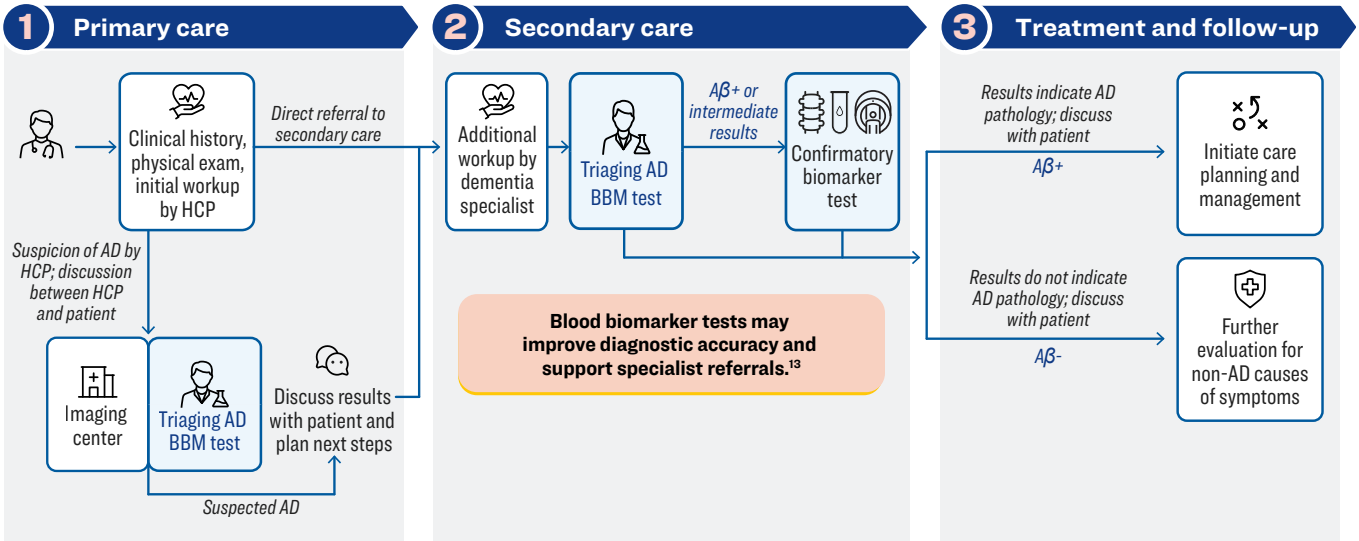
Modified from Schindler SE, et al.[9]

Why Predictive Values Matter for Blood Biomarker Tests

Predictive values indicate the likelihood that blood biomarker test results accurately reflect the presence or absence of amyloid pathology. Their values depend on the prevalence of amyloid pathology in the tested population.[9]

This matters because the same biomarker test performs differently across patients. In a 75-year-old patient with clinical symptoms of AD dementia, where pre-test probability is high (85%), a positive result is highly reliable, with a 98% chance of being a true positive. In contrast, in a 60-year-old patient with subjective cognitive decline and low pre-test probability (20%), positive results are less definitive (31% are false positives).[11]

Example workflow for incorporating blood biomarker tests[12]



Phrasing modified from Mielke MM, et al.[12] with callout added from Palmqvist S, et al.[13]

Examples of commercially available plasma assays in the United States

FDA-cleared tests that meet the CEOi criteria for confirmatory use

For a comprehensive list of commercially available blood biomarker tests for use in clinical practice, please visit the CEOi website.[14]

Company	Test name	Measures	More information
C_2N Diagnostics[15]	PrecivityAD2® Plasma	Aβ42/Aβ40, %P-tau217	FDA-cleared for adults aged ≥40 years with signs or symptoms of cognitive impairment, to aid in identifying amyloid pathology[15]
Fujirebio[16]	Lumipulse® G pTau 217/β-Amyloid 1-42 Plasma Ratio	P-tau217/Aβ42	FDA-cleared for patients aged ≥55 years with cognitive decline presenting to specialized care to confirm AD pathology[17]
Roche Diagnostics[18]	Elecsys® Phospho-Tau (217P) Plasma	P-tau217	FDA-cleared for individuals aged ≥55 years with signs, symptoms, or complaints of cognitive decline, to aid in identifying amyloid pathology[18]

This list includes commercially available tests. Inclusion on this list does not represent an endorsement, referral, or recommendation. All trademarks are property of their respective owners.

Summary and key considerations

- Timely diagnosis is an unmet need in AD[1]
- Blood biomarker tests provide a clinical tool to detect AD-related pathology to support early diagnosis and treatment planning[12]
- Biomarker tests used to confirm AD pathology should be FDA-cleared and meet the confirmatory criteria of ≥90% sensitivity and ≥90% specificity for single cut-point tests, or ≥90% sensitivity, ≥90% specificity, and ≤20% intermediate results for dual cut-point tests[8,9]
- Fluid biomarkers are one component of a clinical evaluation that can be used alongside PET, MRI, and other clinical assessments to support timely diagnosis for patients with cognitive impairment[9]

Consider taking steps now to support your patients' future cognitive health.

Learn more at medical.lilly.com/us/diseases/cognitivehealth



*The Global CEOi BBM Workgroup is a partnership consisting of individuals in academia who help validate blood biomarker tests and diagnostics, the medical device companies that develop them, pharmaceutical companies developing treatment pathways where blood biomarkers may be useful, and patient advocacy groups that aim to improve AD care and treatment. Together, CEOi works to address major challenges in the field of AD.[9]

BBM=blood biomarker. CSF=cerebrospinal fluid. FDA=U.S. Food and Drug Administration. HCP=healthcare professional. MRI=magnetic resonance imaging. PET=positron emission tomography.

1. Liss JL, et al. *J Intern Med.* 2021;290(2):310-334. **2.** Kusoro O, et al. *Int J Geriatr Psychiatry.* 2025;40:e70129. **3.** Alzheimer's Association. *Alzheimers Dement.* 2025;21:e70235. **4.** Alzheimer's Disease International. World Alzheimer Report 2021: Journey through the diagnosis of dementia. Accessed October 12, 2026. https://www.alzint.org/u/World-Alzheimer-Report-2021.pdf **5.** Jansen WJ, et al. *JAMA Neurol.* 2022;79(3):228-243. **6.** Jack CR, et al. *Alzheimers Dement.* 2018;14(4):535-562. **7.** Jack CR, et al. *Alzheimers Dement.* 2024;20(8):5143-5169. **8.** Palmqvist S, et al. *Alzheimers Dement.* 2025;21:e70535. **9.** Schindler SE, et al. *Nat Rev Neurol.* 2024;20(7):426-439. **10.** Global CEO Initiative on Alzheimer's Disease. BBM performance standards. Accessed September 24, 2026. https://alzdiagnostichub.org/bbm-performance-standards/ **11.** VandeVrede L, Schindler SE. *Alzheimers Dement.* 2025;21:e14201. **12.** Mielke MM, et al. *Alzheimers Dement.* 2024;20:8216-8224. **13.** Palmqvist S, et al. *JAMA.* 2024;332(15):1245-1257. **14.** Global CEO Initiative on Alzheimer's Disease. The Alzheimer's Diagnostic Database. Accessed September 24, 2026. https://alzdiagnostichub.org/database/ **15.** C_2N Diagnostics. FDA clears C_2N Diagnostics' PrecivityAD2® — first Alzheimer's blood test for adults with cognitive symptoms as young as 40. Published August 20, 2026. Accessed October 12, 2026. https://c2n.com/news-releases/bg2ziqcz39o3wxf5uc04u279ziw0yv **16.** Fujirebio. Lumipulse® G pTau 217/β-Amyloid 1-42 Plasma Ratio. Accessed September 24, 2026. https://www.fujirebio.com/en-us/products-solutions/lumipulser-g-ptau-217bamyloid-142-plasma-ratio **17.** The Food and Drug Administration. FDA clears first blood test used in diagnosing Alzheimer's disease. Published May 16, 2025. Accessed September 24, 2026. https://www.fda.gov/news-events/press-announcements/fda-clears-first-blood-test-used-diagnosing-alzheimers-disease **18.** Roche Diagnostics. Elecsys® Phospho-Tau (217P) Plasma. Accessed September 24, 2026. https://diagnostics.roche.com/global/en/products/lab/elecsys-pt217p-pid00001120.html

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