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

Timely diagnosis is an unmet need in AD[1]

DIAGNOSED TOO LATE	AD diagnosis is delayed an average of 3.6 years after symptom onset[2]
UNDERDIAGNOSED	Dementia is often undiagnosed, and only 8% of older Americans with MCI receive a diagnosis[3]
MISDIAGNOSED	Both autopsy studies and clinical trials have previously found that 15-30% of individuals diagnosed with Alzheimer's dementia during life did not have AD-related brain pathology[3]

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[4,5]

Who is eligible for blood biomarker testing?

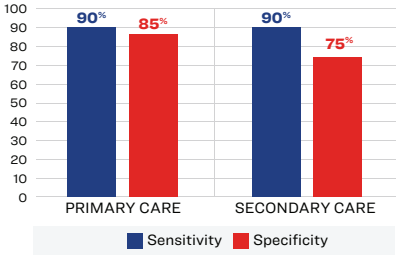
Clinical guidelines and recommendations for the use of blood biomarker tests, including those from the Alzheimer's Association (guidelines) and the Global CEO Initiative Blood-Based Biomarker (BBM) Workgroup* (recommendations), suggest that blood biomarker testing may be considered for individuals with 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.[6,7]

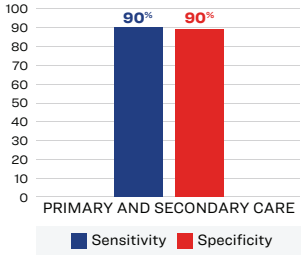
Consider performance standards when selecting blood biomarker tests[7,8]

- 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 CEO Initiative (CEOi) BBM Workgroup has published recommendations for AD blood biomarker tests in clinical use
  - Blood biomarker tests can be used
    - As triaging tools with subsequent confirmatory testing
    - To confirm disease pathology without further PET or CSF testing
  - For triaging, tests should have a sensitivity ≥90% and a specificity of ≥85% in primary care settings or 75% in secondary care settings
  - When used as a confirmatory tool, performance standards should be equivalent to CSF tests (≥90% sensitivity and specificity)

Global CEOi recommendations for blood biomarker tests[7,8]

Triage test	Confirmation test
Purpose: To identify individuals with a high likelihood of amyloid pathology; a second test would be needed to confirm	**Purpose:** To confirm amyloid pathology when interpreted in the context of all clinical findings
Minimum Accuracy Required:	**Minimum Accuracy Required:**

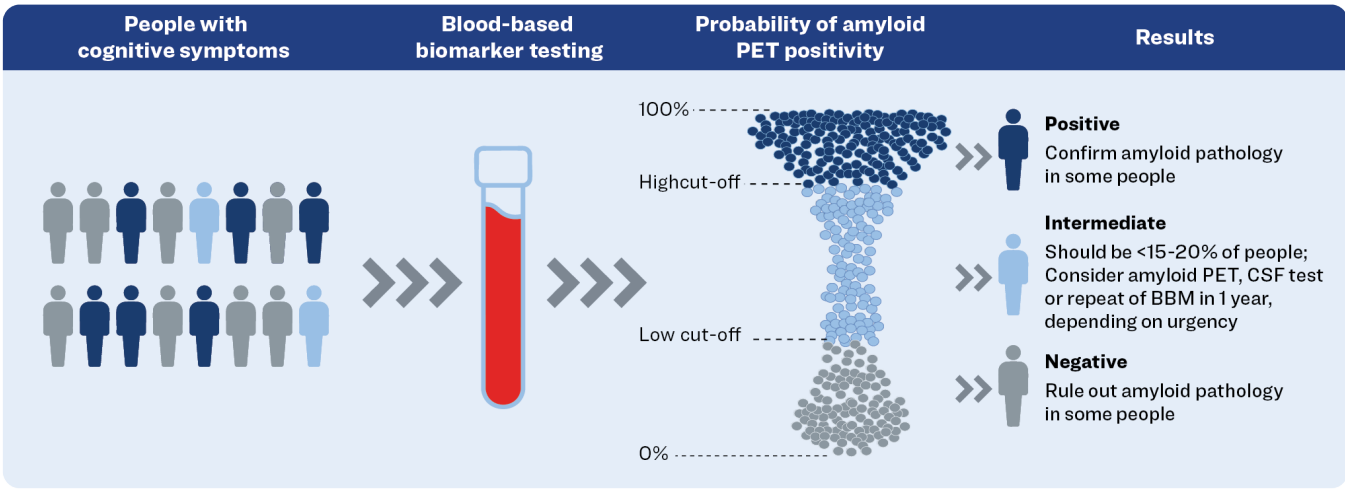




Some tests use a 2-cutoff approach which may improve accuracy in amyloid status classification. This approach should return intermediate values for ≤15-20% of a typical clinical population.

Interpreting blood biomarker test results in primary care

The use of a two cut-off approach leads to three categories of results[7]



Modified from[7]

Why Predictive Values Matter for Blood Biomarker Tests

Positive and negative 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.[7]

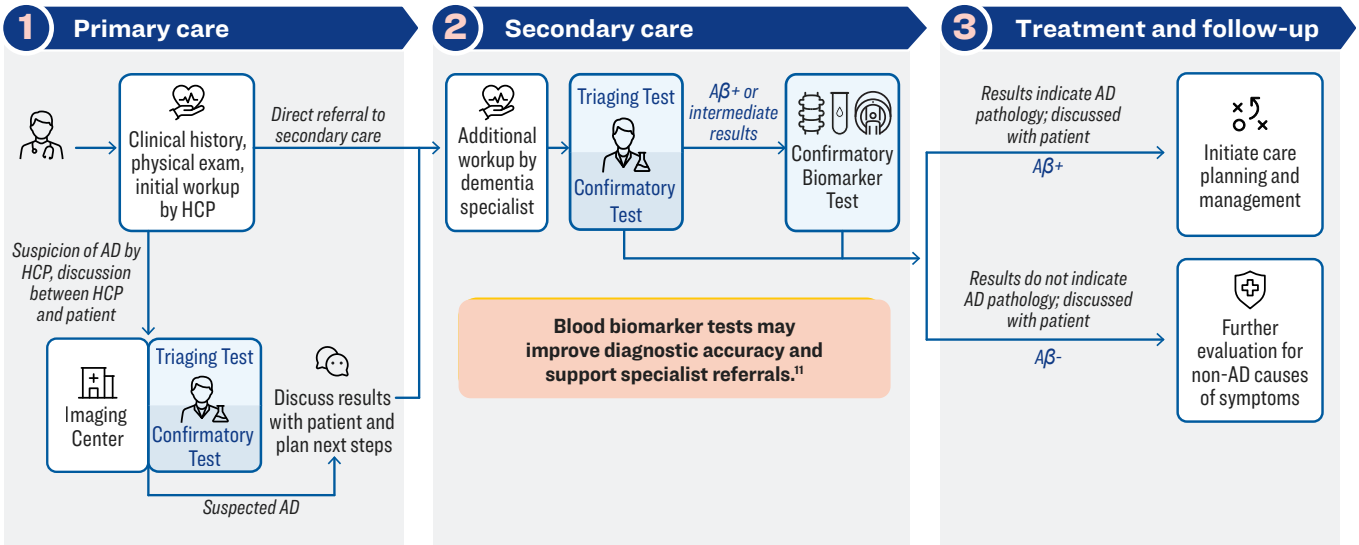
This matters because the same biomarker test performs differently across patients. In a 75-year-old with clinical symptoms of AD dementia, where pre-test probability is high (85%), a positive result is highly reliable, with a 98% chance of being a true positive, but a negative result still carries a meaningful risk of being false (39%). In contrast, in a 60-year-old with subjective cognitive decline and low pre-test probability (20%), positive results are less definitive (31% are false positives), while negative results are reassuring, with a 97% chance of being a true negative.[9]

Interpretation of assays meeting performance criteria for a triaging test[7]:

Result	Interpretation	Potential next steps
Positive	Supports increased likelihood of having AD pathology	Consider referral to secondary care for confirmatory testing
Intermediate	Does not provide a clear answer regarding the status of AD pathology	If greater certainty is needed in the short term, consider an amyloid PET or CSF test; if these tests are unavailable or not needed for immediate management, repeating the test in a year may be reasonable
Negative	Supports absence of AD pathology in most patients	Consider further assessment for alternative causes of cognitive impairment

While triaging blood tests are useful for prioritizing individuals with a high likelihood of amyloid pathology, high-performing blood tests may be used to confirm amyloid pathology without the need for additional testing.[7]

Example workflow for incorporating blood biomarker tests[10]



Modified from[10]

Examples of commercially available plasma assays in the United States

The AD Blood Test Performance Database[12] is a publicly available tool that can be used to view how the performance data of some available tests compare to the Global CEOi BBM Workgroup recommendations.

Company	Test name	Measures	More information
Quest Diagnostics[13]	AD-Detect® Beta-Amyloid 42/40 Plasma Ratio	Aβ42/Aβ40	
C_2N Diagnostics[14]	PrecivityAD® Plasma	Aβ42/Aβ40, APOE	
C_2N Diagnostics[15]	PrecivityAD2™ Plasma	Aβ42/Aβ40, %P-tau217	
Fujirebio[16]	Lumipulse® G ptau217/β-amyloid 1-42 Plasma Ratio	P-tau217/Aβ42	FDA-cleared for patients aged ≥55 with cognitive decline presenting to specialized care to confirm AD pathology[17]
Labcorp[18]	pTau-217/Beta Amyloid 42 Plasma Ratio	P-tau217/Aβ42	
ARUP Laboratories[19]	Phospho-Tau 217 Plasma	P-tau217	
Neurocode[20]	ALZpath Dx: p-Tau 217 Plasma	P-tau217	
Roche Diagnostics[21]	Elecsys® pTau181 Plasma	P-tau181	FDA-cleared for patients aged ≥55 with cognitive decline presenting to primary care to rule out AD pathology[22]

This list only includes some commercially available tests. Inclusion on this list does not represent an endorsement, referral, or recommendation. Because this list only includes some information about a subset of commercially available tests, it cannot be used to compare assay performance to CEOi acceptable performance criteria. 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[10]
- Biomarker tests used to confirm AD pathology should have performance equivalent to FDA-cleared CSF tests[7]
- 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[7]

*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.[7]

APOE=apolipoprotein E. CSF=cerebrospinal fluid. FDA=U.S. Food and Drug Administration. HCP=healthcare professional. MCI=mild cognitive impairment. 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 Psychiatr.* 2025;40:e70129. **3.** Alzheimer's Association. *Alzheimers Dement.* 2025;21:e70235. **4.** Jack CR, et al. *Alzheimers Dement.* 2018;14(4):535-562. **5.** Jack CR, et al. *Alzheimers Dement.* 2024;20(8):5143-5169. **6.** Palmqvist S, et al. *Alzheimers Dement.* 2025;21:e70535. **7.** Schindler SE, et al. *Nat Rev Neurol.* 2024;20(7):426-439. **8.** Global CEO Initiative on Alzheimer's Disease. BBM Performance Standards. Accessed March 8, 2026. https://alzdiagnostichub.org/bbm-performance-standards/ **9.** VandeVrede L, Schindler SE. *Alzheimers Dement.* 2025;21:e14201. **10.** Mielke MM, et al. *Alzheimers Dement.* 2024;20:8216-8224. **11.** Palmqvist S, et al. *JAMA*. 2024;332(15):1245-1257. **12.** Global CEO Initiative on Alzheimer's Disease. The Alzheimer's Diagnostic Database. Accessed April 21, 2026. https://www.alzbiomarkerhub.org/performance-database-tool **13.** Quest Diagnostics. Quest AD-Detect® Beta-Amyloid 42/40 Ratio, Plasma. Accessed February 20, 2026. https://testdirectory.questdiagnostics.com/test/test-detail/11786/quest-ad-detect-beta-amyloid-4240-ratio-plasma?cc=MASTER **14.** C2N Diagnostics. Precivity AD. Accessed February 20, 2026. https://precivityad.com/healthcare-providers **15.** C2N Diagnostics. Precivity AD2. Accessed February 20, 2026. https://precivityad.com/precivityad2-hcp **16.** Fujirebo. Lumipulse G pTau 217/β-Amyloid 1-42 Plasma Ratio. Accessed February 20, 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 January 12, 2026. https://www.fda.gov/news-events/press-announcements/fda-clears-first-blood-test-used-diagnosing-alzheimers-disease **18.** Labcorp. Advancing the evaluation of amyloid pathology with pTau-217/Beta Amyloid 42 ratio. Accessed February 20, 2026. https://www.labcorp.com/education-events/articles/advancing-evaluation-amyloid-pathology-ptau-217beta-amyloid-42-ratio **19.** ARUP laboratories. Phospho-Tau 217, Plasma. Accessed February 20, 2026. https://ltd.aruplab.com/Tests/Pub/3019017 **20.** Neurocode. ALZpath Dx: Plasma Phosphorylated Tau 217 (p-Tau 217). Accessed February 23, 2026. https://neurocode.com/test/alzpath-plasma-phosphorylated-tau-217/ **21.** Roche Diagnostics. Our first Roche Blood Based Biomarker dedicated to stratifying patients evaluated for Alzheimer's Disease: Elecsys® Phospho-Tau (181P) Plasma. Accessed February 20, 2026. https://diagnostics.roche.com/us/en/products/lab/elecsys-phospho-tau-181p-plasma-pid00001042.html **22.** Roche Diagnostics. Roche's Elecsys pTau181 becomes the only FDA-cleared blood test for use in primary care to rule out Alzheimer's-related amyloid pathology. Published October 13, 2025. Accessed February 20, 2026. https://diagnostics.roche.com/us/en/news-listing/2025/fda-cleared-ptau181-alzheimers-blood-test.html