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FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2025

ALZHEIMER'S ASSOCIATION RELEASES ITS FIRST CLINICAL PRACTICE GUIDELINE FOR BLOOD-BASED BIOMARKER TESTS

Key Takeaways

- **At AAIC 2025, the Alzheimer's Association released the first in a series of clinical practice guidelines for the diagnosis, treatment and care of Alzheimer's and all other dementia.**
- **The guideline focuses on the use of blood-based biomarker tests by specialists to assess levels of Alzheimer's disease pathology in people with cognitive impairment.**
- **The Alzheimer's Association provides evidence-based resources to help clinicians identify the disease early and ensure patients receive the right treatment as quickly as possible.**
- **These and other planned guidelines are part of ALZPro™, the Alzheimer's Association's centralized hub for resources, support and information for dementia professionals.**

TORONTO, July 29, 2025 — In a landmark step toward transforming Alzheimer's disease diagnosis in specialty care, the Alzheimer's Association today released its first clinical practice guideline (CPG) on the use of blood-based biomarker (BBM) tests. The guideline is being reported at the Alzheimer's Association International Conference® 2025 (AAIC®) in Toronto and online, and published in *Alzheimer's & Dementia®: The Journal of the Alzheimer's Association*.

The CPG provides clear evidence-based, brand-agnostic recommendations to support more accurate and accessible diagnosis of Alzheimer's using blood-based biomarker tests. The recommendations are linked to a systematic review using a robust and transparent methodology, and will be updated regularly as evidence evolves.

"This is a pivotal moment in Alzheimer's care," said Maria C. Carrillo, Ph.D., Alzheimer's Association chief science officer and medical affairs lead, and a co-author of the guideline. "For the first time, we have a rigorously evidence-based guideline that empowers clinicians to use blood biomarker tests confidently and consistently. Adoption of these recommendations will lead to quicker, more accessible, more accurate diagnoses — and better outcomes for individuals and families affected by Alzheimer's."

The recommendations in the new CPG — both of which apply only to patients with cognitive impairment being seen in specialized care for memory disorders — are:

- BBM tests with ≥90% sensitivity and ≥75% specificity can be used as a triaging test, in which a negative result rules out Alzheimer's pathology with high probability. A positive result should also be confirmed with another method, such as a cerebral spinal fluid (CSF) or amyloid positron emission tomography (PET) test.
- BBM tests with ≥90% for both sensitivity and specificity can serve as a substitute for PET amyloid imaging or CSF Alzheimer's biomarker testing.

The guideline cautions that there is significant variability in diagnostic test accuracy and many commercially available BBM tests do not meet these thresholds.

"Not all BBM tests have been validated to the same standard or tested broadly across patient populations and clinical settings, yet patients and clinicians may assume these tests are interchangeable," said Rebecca M. Edelmayer, Ph.D., Alzheimer's Association vice president of scientific engagement and a co-author of the guideline. "This guideline helps clinicians apply these tools responsibly, avoid overuse or inappropriate use, and ensure that patients have access to the latest scientific advancements."

Compared to standard-of-care PET imaging and CSF tests, blood-based biomarkers are typically less costly, more accessible and more acceptable to patients. The guideline emphasizes that BBM tests do not substitute for a comprehensive clinical evaluation by a health care professional, and should be ordered and interpreted by a health care professional in the context of clinical care.

This is the first evidence-based guideline using Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology in the Alzheimer's space. The use of GRADE ensures a transparent, structured and evidence-based process for evaluating the certainty of evidence and formulating recommendations. This strengthens the credibility and reproducibility of the guideline and allows for explicit linkage between evidence and recommendations.

This guideline's primary audience includes specialists involved in the diagnostic evaluation of cognitive impairment in specialized care settings. A specialist is defined as a health care provider, typically in neurology, psychiatry or geriatrics, who cares for adults with cognitive impairment or dementia. It also applies to primary care providers, nurse practitioners and physician assistants in specialized care settings.

A panel of 11 clinicians convened by the Alzheimer's Association — including clinical neurologists, geriatricians, nurse practitioners, physician assistants and subject-matter experts — conducted a systematic review and formulated evidence-based recommendations for using blood-based biomarkers in individuals with objective cognitive impairment, including those with mild cognitive impairment (MCI) or dementia. Final recommendations were informed by public comments and input from the Association's National Early-Stage Advisory Group, which includes people living with early-stage Alzheimer's.

For this initial iteration of the guideline, the BBMs included plasma phosphorylated-tau (p-tau) and amyloid-beta (Aβ) tests measuring the following analytes: p-tau217, ratio of p-tau217 to non-p-tau217 ×100 (%p-tau217), p-tau181, p-tau231, and ratio of Aβ42 to Aβ40. The various BBM tests measure abnormal forms of either amyloid beta or tau protein, the two biomarkers associated with Alzheimer's disease. Forty-nine (49) observational studies were reviewed and 31 BBM tests were evaluated.

The panel determined that endorsing specific tests was premature, opting for a brand-agnostic, performance-based approach that blinded panel members to the tests they were evaluating to minimize bias. This ensures the guideline's credibility, durability and actionability. According to the panel: "Ranking or endorsing specific tests is premature at this time. Instead, test accuracy data and accuracy judgments reported in this guideline are meant to serve as a resource for clinicians … to aid them in choosing which test(s) to order."

The panel formulated two recommendations and one Good Practice Statement for the use of BBM tests in the diagnostic workup of patients with objective cognitive impairment being seen in specialized care.

- Recommendation 1 — In patients with objective cognitive impairment presenting for specialized memory-care, the panel suggests using a high-sensitivity BBM test as a triaging test in the diagnostic workup of Alzheimer's disease.
- Recommendation 2 — In patients with objective cognitive impairment presenting for specialized memory care, the panel suggests using a high-sensitivity and high-specificity BBM test as a confirmatory test in the diagnostic workup of Alzheimer's disease.
- Good Practice Statement — A BBM test should not be obtained before a comprehensive clinical evaluation by a health care professional, and test results should always be interpreted within the clinical context. The panel urges clinicians to consider the pre-test probability of Alzheimer's disease pathology for each patient when deciding whether or not to use a BBM test.

This CPG is part of ALZPro™, the Alzheimer's Association's comprehensive hub of resources to promote best practices, empowering health professionals across disciplines to reduce risk, advance early detection, improve care and expand equitable access for all communities. ALZPro unites care resources, relevant scientific findings, clinical guidelines and insights, continuing education and implementation tools on one platform.

Upcoming clinical practice guidelines will address cognitive assessment tools (Fall 2025), clinical implementation of staging criteria and treatment (2026) and prevention of Alzheimer's and other dementias (2027). This clinical practice guideline was convened and funded by the Alzheimer's Association, but the Association was not involved in formulating the clinical questions or recommendations.

About the Alzheimer's Association International Conference® (AAIC®)
The Alzheimer's Association International Conference (AAIC) is the world's largest gathering of researchers from around the world focused on Alzheimer's and other dementias. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.
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About the Alzheimer's Association®
The Alzheimer's Association is a worldwide voluntary health organization dedicated to Alzheimer's care, support and research. Our mission is to lead the way to end Alzheimer's and all other dementia — by accelerating global research, driving risk reduction and early detection, and maximizing quality care and support. Our vision is a world without Alzheimer's and all other dementia®. Visit alz.org or call 800.272.3900.

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Session: Evidence-Based Clinical Practice Guidelines for Detection and Diagnosis of Cognitive Impairment using Blood-based Biomarkers and Cognitive Testing: Two Guideline Initiatives from the Alzheimer's Association

Proposal ID: 108894
Oral Presentation: Tuesday, July 29, 2025: 2:00 P.M.-3:30 P.M. EDT (3-21-DEV)

Clinical practice guideline for blood-based biomarkers in the diagnostic workup of Alzheimer's disease within specialized care settings: A report from the Alzheimer's Association

Background: In recent years, blood-based biomarkers (BBMs) have transformed the diagnostic landscape of Alzheimer's disease (AD), with some now approaching readiness for clinical implementation. This progress aligns with the growing importance of accurate early diagnostics and availability of anti-Aβ therapies for the treatment of early symptomatic AD, reinforcing the need for more rapid and early diagnostic capabilities. To address this need, the Alzheimer's Association convened a multidisciplinary panel of clinical experts, subject-matter specialists, and guideline methodologists to conduct a systematic review and develop evidence-based recommendations for the use of BBMs in the diagnostic evaluation of AD. The scope of this guideline is focused on individuals with cognitive impairment - either MCI or dementia - who are undergoing diagnostic assessment in secondary or tertiary care settings.
Method: The panel conducted a systematic review to assess BBMs' diagnostic test accuracy in detecting amyloid pathology for triaging (≥90% sensitivity, ≥75% specificity) and confirmatory (≥90% sensitivity and specificity) diagnostic workup. The BBMs of interest included plasma p-tau and Aβ tests measuring the following analytes: p-tau217, %p-tau217, p-tau181, p-tau231, and Aβ42/Aβ40 ratio. The reference standard tests included CSF, amyloid PET, or neuropathology examination. The panel applied the GRADE approach to assess the certainty of the evidence and the GRADE Evidence-to-Decision Framework to develop its recommendations.
Result: Across 49 observational studies meeting eligibility criteria, 31 different BBM tests were evaluated. Using predefined decision thresholds, the panel determined whether each test has 1) sufficient diagnostic test accuracy to be used as a triaging test where a positive test is to be confirmed by PET or CSF, 2) sufficient diagnostic test accuracy as a confirmatory test to replace PET or CSF, or 3) insufficient diagnostic test accuracy to recommend current use in clinical practice. Recommendations will be provided in case any BBMs met a priori DTA thresholds.
Conclusion: BBMs can improve early AD diagnosis and expand access to disease-modifying therapies. Evidence-based guidelines are key to standardizing their use and will be updated as new evidence and applications emerge.

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