UNDERSTANDING AND COMMUNICATING BLOOD BIOMARKER TESTING IN

Alzheimer's Disease

Some media generated by AI

Lilly A MEDICINE COMPANY

UNDERSTANDING AND COMMUNICATING BLOOD BIOMARKER TESTING IN

Alzheimer's Disease

Learning Objectives

1. Explain the role and significance of blood biomarkers (BBMs) in the diagnosis and management of Alzheimer's disease (AD)
2. Understand literature-based considerations for communicating test results to patients and care partners
3. Address psychological and practical considerations in biomarker diagnosis conversations
4. Support informed decision-making and patient-centered care

This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

Lilly A MEDICINE COMPANY

Alzheimer's Disease

Why Blood Biomarkers Matter in Alzheimer's Disease

Alzheimer's disease (AD) affects up to 22% of people aged ≥50 years worldwide,[1] including:

- **69M living with mild cognitive impairment (MCI)[a]**
- **32M living with amyloid-positive AD dementia**

AD starts long before symptoms present.[2] While PET and CSF tests are highly accurate,[3] they may be costly, invasive, and have limited availability in both a primary and secondary care setting.[4]

The diagnostic gap

Only **4 in 10** individuals aged 65-80 years have had a cognitive screening[5]

Half of patients with AD are not diagnosed until moderate or advanced stages[6]

The role of blood biomarkers (BBMs)

BBMs are less invasive than CSF testing and may be more accessible than PET in some settings.[7]

Under current guidelines, the selection of diagnostic modality should be guided by clinical judgement and context.[2,8]

Considerations for care providers[9]

Interpret BBM results within clinical context | **Counsel patients with empathy and clarity** | **Incorporate BBMs into shared decision-making** | **Refer patients to specialty care as needed**

Use of highly accurate **BBM tests may reduce the need for PET and CSF testing.[10]**

This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

[a]Diagnosis of MCI does not typically include confirmatory amyloid testing.

AD=Alzheimer's Disease; BBM=Blood Biomarker; CSF=Cerebrospinal Fluid; MCI=Mild Cognitive Impairment; PET=Positron Emission Tomography.

Lilly A MEDICINE COMPANY

Alzheimer's Disease

Pathophysiology and Diagnosis of Alzheimer's Disease

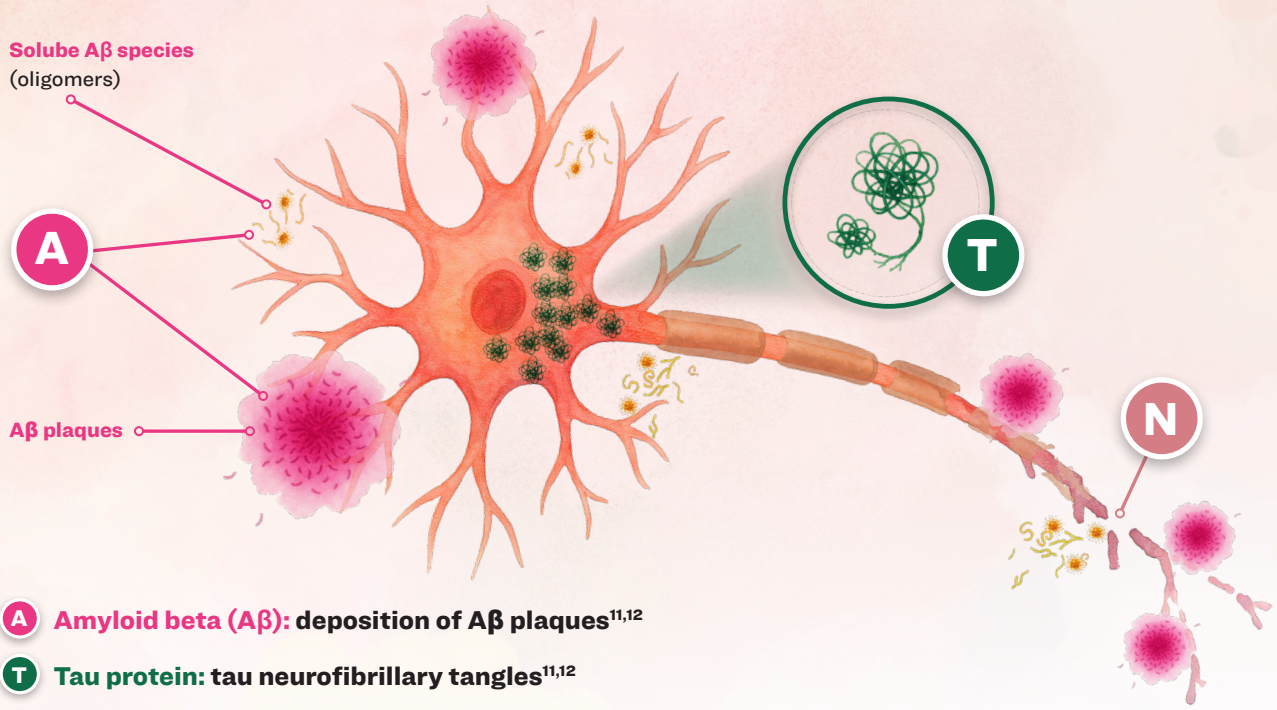
AD is a progressive neurodegenerative disorder characterized by hallmark pathophysiological features that emerge years before symptoms.[2]

What happens in the brain[11,12]

Aβ plaques form **outside** neurons

Tau NFTs form **inside** neurons

Neuroinflammation and neuronal death



- **A** **Amyloid beta (Aβ):** **deposition of Aβ plaques**[11,12]
- **T** **Tau protein:** **tau neurofibrillary tangles**[11,12]
- **N** **Neuroinflammation:** **neuronal injury and neurodegeneration**[11,12]

Some media generated by AI
Figure not drawn to scale

Progression of the neuropathological burden leads to the later appearance and progression of clinical symptoms, such as decline in cognitive function.[11]

This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

Aβ=Amyloid Beta; AD=Alzheimer's Disease; NFT=Neurofibrillary Tangle.

Lilly A MEDICINE COMPANY

Alzheimer's Disease

Pathophysiology and Diagnosis of Alzheimer's Disease

Several types of tests may be used during AD diagnosis, including PET scans, CSF testing, and BBM testing.[2]

Both cognitive assessment and neuropathologic changes are required to diagnose AD

Cognition:

– MMSE, MoCA, or similar[a,13]

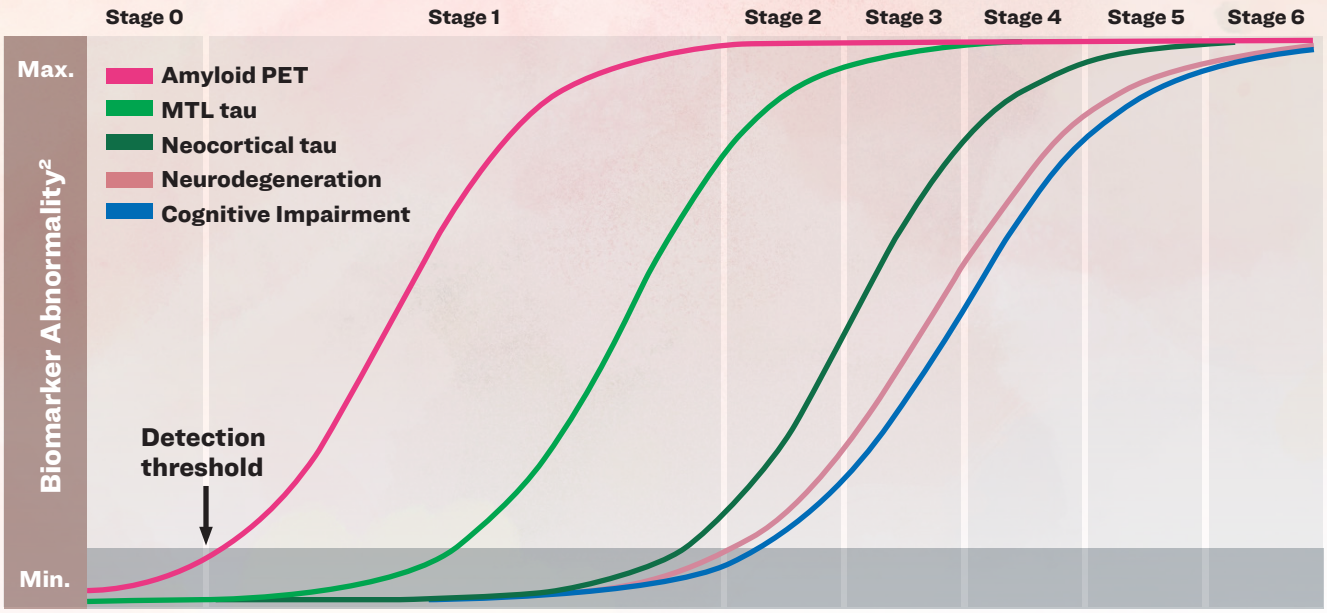
Pathology

– Aβ: PET, CSF, BBMs[2]

– Tau: PET, CSF, BBMs[2]

– Neuroinflammation (GFAP): CSF, BBMs (research use only)[2]

– Neurodegeneration (NfL): CSF, BBMs (research use only)[2]



Pathologic changes precede clinical symptoms by decades.[14]

This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

[a]Please note that this is not an exhaustive list of all cognitive screening tools.

Aβ=Amyloid Beta; AD=Alzheimer's Disease; BBM=Blood Biomarker; CSF=Cerebrospinal Fluid; GFAP=Glial Fibrillary Acidic Protein; MMSE=Mini-Mental State Examination; MoCA=Montreal Cognitive Assessment; MTL=Medial Temporal Lobe; NfL=Neurofilament Light Chain; PET=Positron Emission Tomography.

Lilly A MEDICINE COMPANY

Alzheimer's Disease

Introduction to Blood Biomarkers

BBMs may enable earlier and scalable detection of AD.[15,16]

Core AD-specific biomarkers

Plasma Aβ42/40 ratio: A plasma biomarker reflecting brain amyloid plaque pathology (amyloid status).[2,15]

P-tau181, P-tau217: Tau-derived plasma biomarkers that have strong associations with amyloid proteinopathy and tau pathology[2,15,17]

Non-specific biomarkers

GFAP: A plasma biomarker reflecting astrocytic reactivity and inflammatory processes in the brain; associated with early amyloid pathology[2,15]

NfL: A biomarker of neuronal injury and neurodegeneration, reflecting large-caliber axonal damage; elevated across multiple neurologic conditions rather than AD specificity[2,15]

This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

Aβ=Amyloid Beta; AD=Alzheimer's Disease; BBM=Blood Biomarker; GFAP=Glial Fibrillary Acidic Protein; NfL=Neurofilament Light Chain; P=Phosphorylated.

Lilly A MEDICINE COMPANY

Alzheimer's Disease

How Biomarkers May Help in the Clinic

Biomarkers may enhance clinical care across the diagnostic journey by helping to improve detection, confidence, management, and patient support.[15]

Clinical utility

BBMs may help:

Facilitate earlier detection

- Identify pathology in the symptomatic stages[15]
- Reduce time to accurate diagnosis (especially in atypical presentations)[15,18]

Increase diagnostic accuracy

- Differentiate AD from other neurodegenerative diseases or normal aging[18]
- Higher diagnostic accuracy than standard combined assessment with clinical examination, cognitive testing, and a CT scan[19]

Improve clinical management

- Reduce need for extensive imaging and neuropsychological assessments, lowering healthcare resource use and burden on patients[20,21]

Support treatment eligibility

- Confirm AD pathology in patients with cognitive impairment[a], which may improve access to services and amyloid-targeting therapies (ATTs) (if eligible)[b,15,22]
- May inform and guide treatment decisions[20]

Benefit patient and care partner(s)

- Provide patients with greater certainty and the ability to plan ahead[21,23]
- Encourage patients to adopt or continue healthy behaviors, such as exercise and cognitive activities[23]
- Enable care partners to fully appreciate future responsibilities[21]
- Spur care partners to connect with support resources[21]

This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

[a]Confirmed with objective cognitive tests; [b]ATTs include donanemab and lecanemab.[24,25]

AD=Alzheimer's Disease; ATT=Amyloid-Targeting Therapy; CT=Computerized Tomography.

Lilly A MEDICINE COMPANY

Alzheimer's Disease

Interpreting BBM Results

BBM results may provide valuable information but must be interpreted with caution.[26]

Key considerations

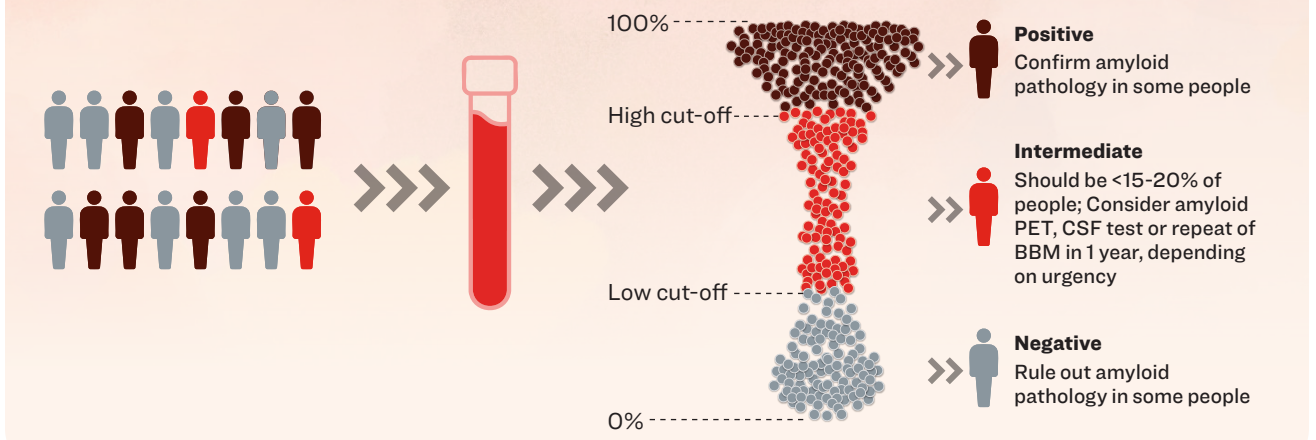
- Comorbidities (e.g., CKD, stroke, or obesity) may influence results[9,26]
- There is limited data on BBM testing in diverse populations[26]
- False positives/negatives may occur – predictive value depends on accurate estimations of AD prevalence[9]

Two-threshold strategy

Can be used to increase overall accuracy and improve utility[9]

- Following testing, patients are classified as negative, intermediate, or positive for AD pathology[9]
- Patients in the intermediate category may then be sent for confirmatory evaluation using orthogonal methods such as PET imaging or CSF testing[9]

The two-threshold strategy may help guide next clinical steps[9]



This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

AD=Alzheimer's Disease; BBM=Blood Biomarker; CKD=Chronic Kidney Disease; CSF=Cerebrospinal Fluid; PET=Positron Emission Tomography.

Lilly A MEDICINE COMPANY

Pre-Testing Considerations

Patient-centered care recommendations from the DETeCD-ADRD guidelines

- Engage patients in shared decision-making[8]
- Work together to establish patient and care partner goals[8]
- Assess the patient's capacity to understand the purpose and implications of results[26]

Considerations for addressing hesitancy with empathy

- Use active listening and validation to identify the source of hesitancy (e.g., stigma, discrimination, psychological trauma)[27]
- Correct misinformation by providing clear, empathetic explanations[27]

Considerations for addressing the implications of proceeding with BBM testing

- Discuss risks, limitations, and real-world implications of biomarker testing, including privacy considerations and the potential for discrimination (e.g., denial of coverage) based on the result[28]
- Provide information about entities (i.e., insurance providers) that may have access to biomarker test results and how these results could be used[28]

These expectation-setting considerations may be useful before ordering a BBM test, and may set the stage for a potential diagnosis conversation.[8,27,28]

This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

BBM=Blood Biomarker; DETeCT-ADRD=Diagnostic Evaluation, Testing, Counseling, and Disclosure of Suspected Alzheimer's Disease and Related Disorders.

Lilly A MEDICINE COMPANY

Post-Testing Considerations

Considerations for adopting responsible transparency

- Use structured conversation supported by visual aids[8,23,28]
- Clearly disclose the syndrome name, likely cause, and disease stage[8]
- Explain the test, results, implications, and next steps using plain, jargon-free language to decrease confusion[8]

Current evidence supports ensuring the understanding of results and their implications

- Elevated biomarkers = increased risk, but does not guarantee progression to dementia[23]
- Negative result does not equal lifetime protection[23]

Considerations for personalized communication strategies

- Acknowledge that some patients may experience short-term distress following the diagnosis conversation[23]
- Tailor delivery to the patient's cognitive status, cultural background, and stigma concerns[8,28]
- Discuss care planning, safety considerations, and treatment options based on current guidelines and clinical judgement, and involve care partners when appropriate[8]

BBM results may complement a comprehensive medical assessment in alignment with current clinical practice guidelines.[9,29]

This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

BBM=Blood Biomarker.

Lilly A MEDICINE COMPANY

Post-Testing Considerations

Research findings have suggested best practices for maintaining communication

- Provide take-home materials with clear follow-up options[30]
- Schedule follow-up visits or phone calls to address new questions[30]

Clinical guidelines recommend connecting the patient and care partners to resources

- Refer to specialists for complex or atypical cases[8]
- Share information on medical, psychosocial, and community support resources[8]

Considerations for a collaborative diagnosis conversation

- Reinforce that the diagnosis conversation is not a one-time event but an evolving dialogue[8]
- Revisit discussions as patient understanding evolves[31]
- Address misinformation and patient hesitancy (e.g., "there's nothing I can do" mindset)[27]

Ongoing support after the diagnosis conversation may improve the patient experience by helping patients and care partners to remain engaged, informed, and connected.[31]

This educational resource is intended for informational purposes only. It does not constitute medical advice or a directive for clinical practice. BBMs are validated for use in symptomatic individuals; use in other populations is not supported by current evidence. All recommendations should be interpreted in the context of published guidelines and individual clinical judgment.

Lilly A MEDICINE COMPANY

References:

1. Gustavsson A, et al. *Alzheimers Dement.* 2023;19(2):658-670.
2. Jack Jr. CR, et al. *Alzheimer's Dement.* 2024;20:5143-5169.
3. Palmqvist S, et al. *Neurology.* 2015;85(14):1240-1249.
4. Teunissen CE, et al. *Lancet Neurol.* 2022;21(1):66-77.
5. https://ihpi.umich.edu/national-poll-healthy-aging/national-findings/detecting-alzheimers-disease-older-adults-experiences (Accessed October 7, 2025).
6. Alzheimer's disease facts and figures. *Alzheimers Dement.* 2025;21(4):e70235.
7. Hampel H, et al. *Nat Rev Neurol*. 2018;14(11):639-652.
8. Atri A, et al. *Alzheimers Dement.* 2024;21(6):e14333.
9. Schindler SE, et al. *Nat Rev Neurol.* 2024;20(7):426-439.
10. Barthélemy NR, et al. *Nat Med.* 2024;30(4):1085-1095.
11. DeTure MA, Dickson DW. *Mol Neurodegener.* 2019;14(1):32.
12. Hansson O. *Nat Med.* 2021;27(6):954-963.
13. Trzepacz PT, et al. *BMC Geriatr*. 2015;15:107.
14. Jack Jr. CR, et al. *Lancet Neurol.* 2010;9(1):119-128.
15. Dubois et al. *Alzheimers Res Ther.* 2023;15:175.
16. https://alzdiagnostichub.org/blood-test-performance-database/ (Accessed December 11, 2025).
17. Lai R, et al. *Biomedicines.* 2024;12(8):1836.
18. Andersen E, et al. *Biomark Neuropsychiatry.* 2021;5(3):100041.
19. Palmqvist S, et al. *JAMA*. 2024;332:1245-1255.
20. Patel KJ, et al. *Alzheimers Dement* (N Y). 2024;10(2):e12464.
21. Patel KJ, et al. *Alzheimers Dement* (N Y). 2024;10(2):e12463.
22. Porteri C, et al. *Neurobiol Aging.* 2017;52:132-140.
23. Ketchum FB, et al. *J Prev Alz Dis.* 2024;6(11):1572-1580.
24. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761248s004lbl.pdf (Accessed October 7, 2025).
25. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761269s013lbl.pdf (Accessed October 7, 2025).
26. Mielke MM, et al. *Alzheimers Dement.* 2024;20(11):8216–8224.
27. Wilkenfeld DA, et al. *Neurotherapeutics.* 2021;18(2):673–685.
28. Mielke MM, et al. *Alzheimers Dement.* 2024;20(11):8209–8215.
29. Palmqvist S, et al. *Alzheimers Dement.* 2025;21(7):e70535.
30. Lingler JH, et al. *J Alzheimers Dis.* 2016;52(1):17-24.
31. Wollney EN, et al. *PEC Innov.* 2024;4:100253.