UNDERSTANDING AND COMMUNICATING BLOOD BIOMARKER TESTING IN

Alzheimer's Disease



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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.

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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]**

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[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.

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Alzheimer's Disease

Pathophysiology and Diagnosis of Alzheimer's Disease

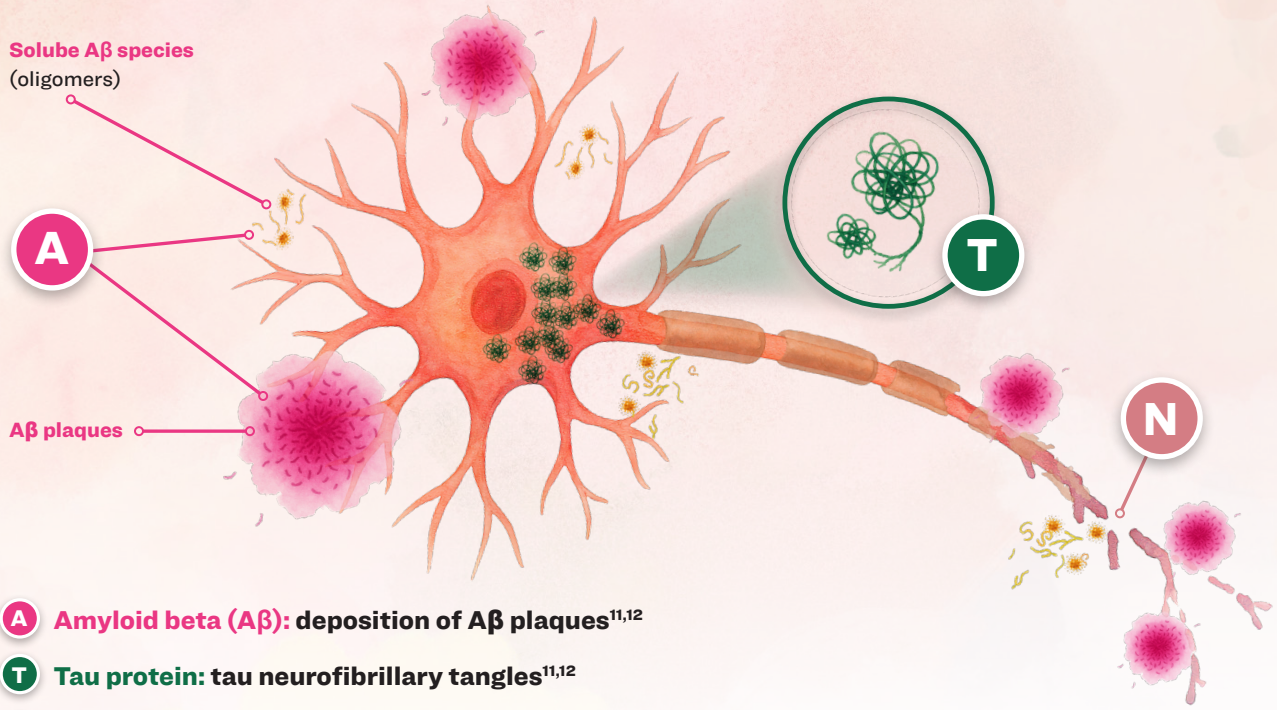
AD is a progressive neurodegenerative disorder characterized by hallmark pathophysiological features that emerge years before symptoms.[2]

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]

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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]

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

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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]

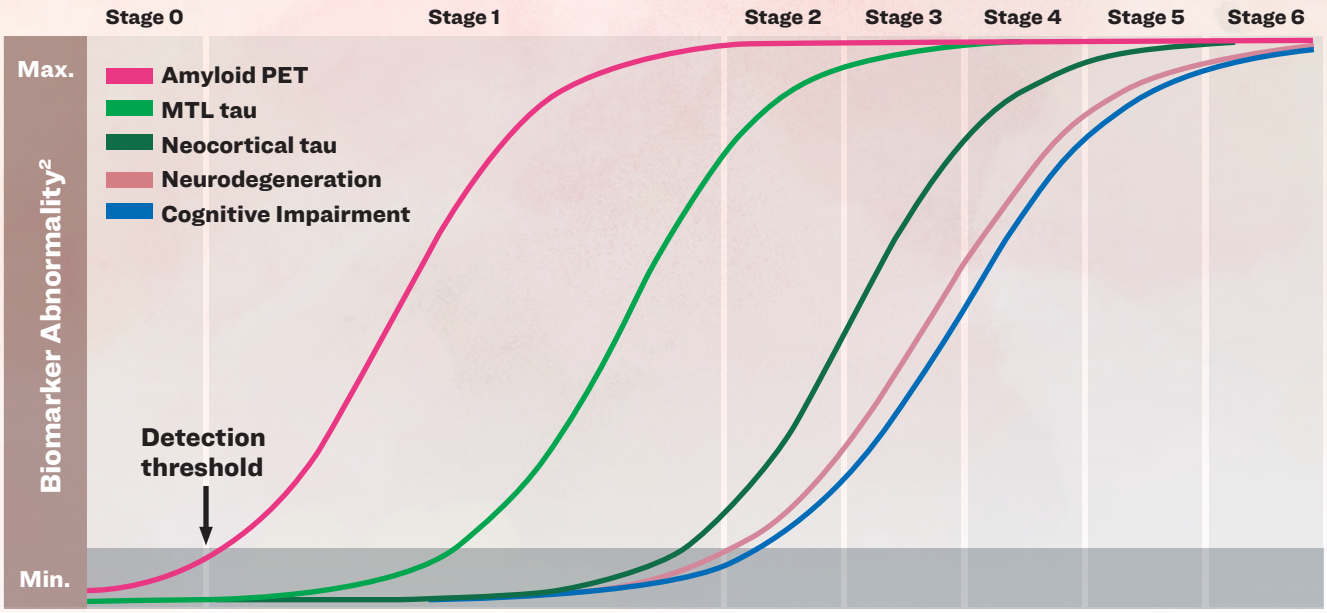
Pathology

– 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]

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[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.

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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]

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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]

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[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.

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Alzheimer's Disease

Interpreting BBM Results

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

Key considerations

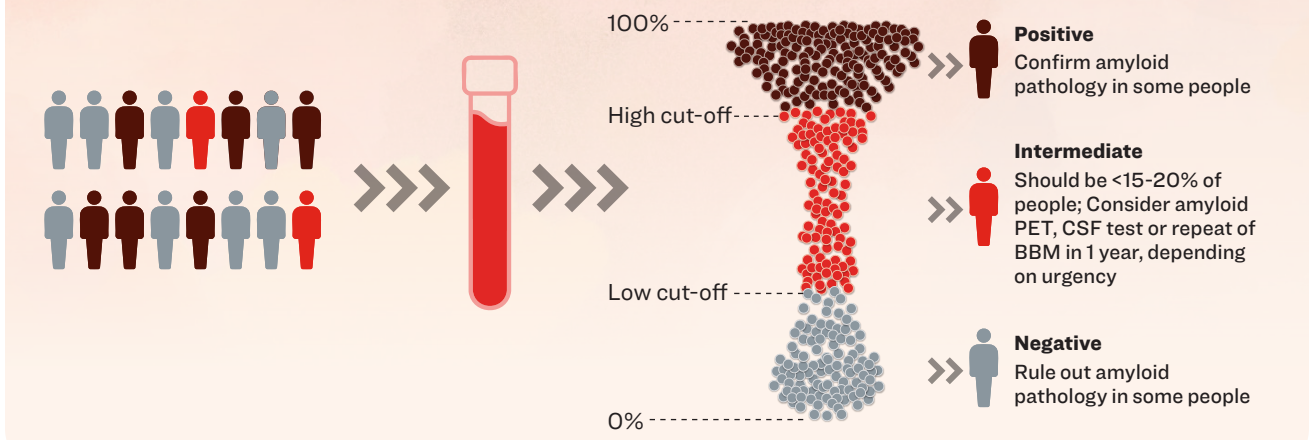
- Comorbidities (e.g., CKD, stroke, or obesity) may influence results[9,26]
- There is limited data on BBM testing in diverse populations[26]
- False positives/negatives may occur – predictive value depends on accurate estimations of AD prevalence[9]

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]



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

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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]

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

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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]

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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]

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