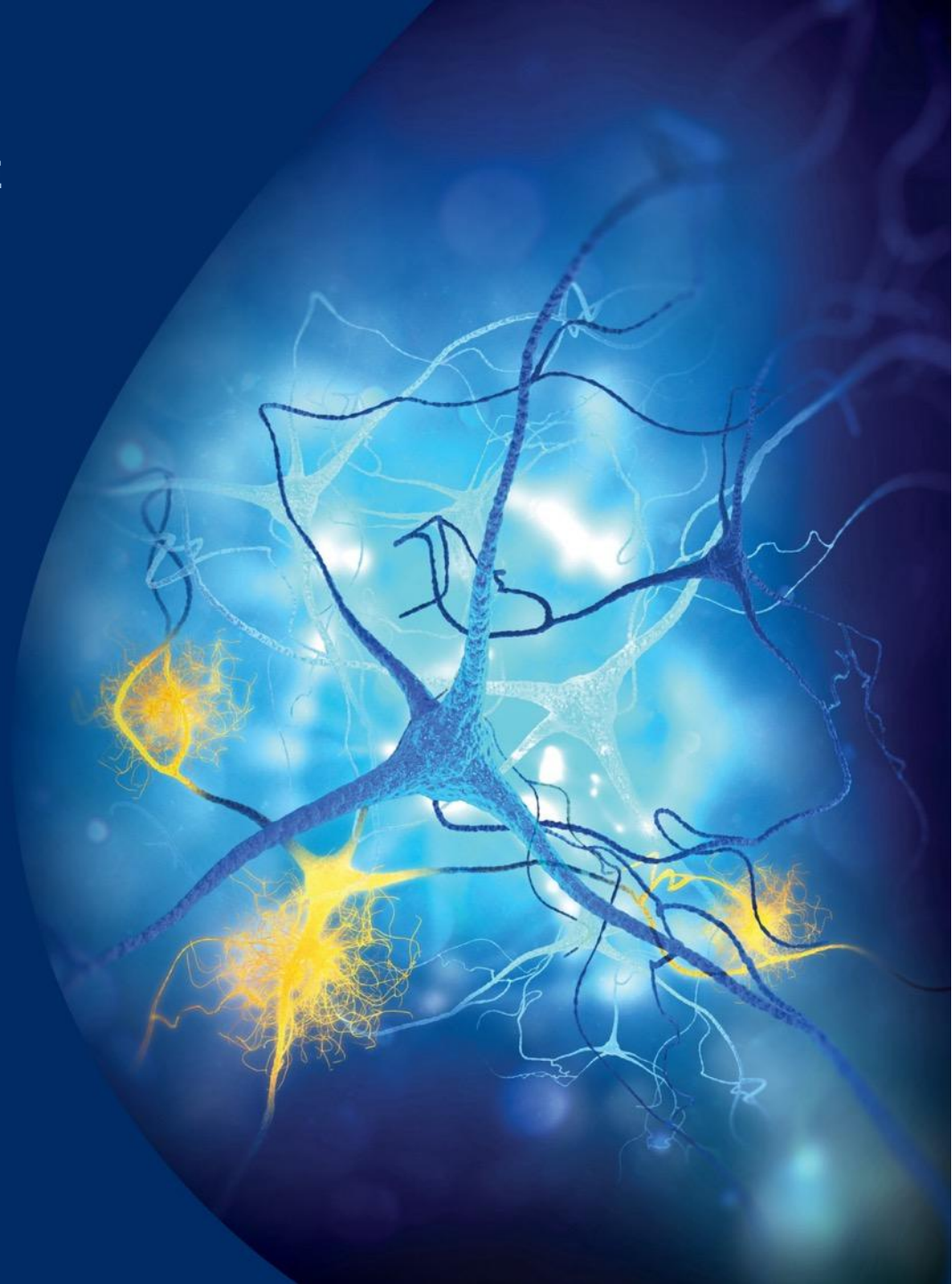
PRACTICAL APPLICATIONS

Complimentary Accredited 3-Part Webinar Series | **PART ONE**

Demystifying Alzheimer's Blood Biomarkers

What Every Clinician Needs to Know



Tuesday, December 9, 2025

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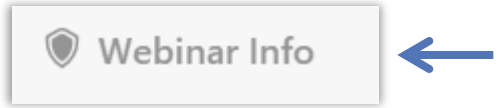

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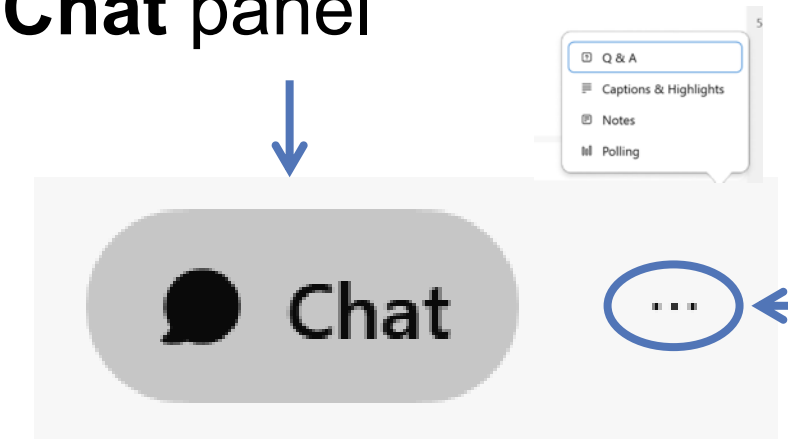

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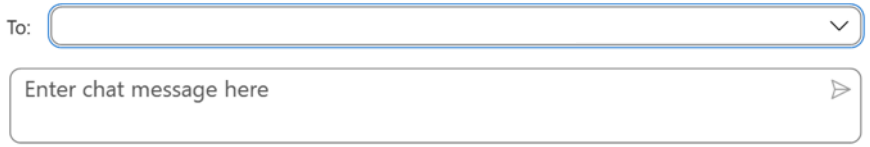

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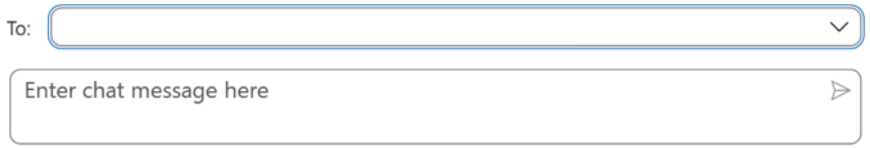

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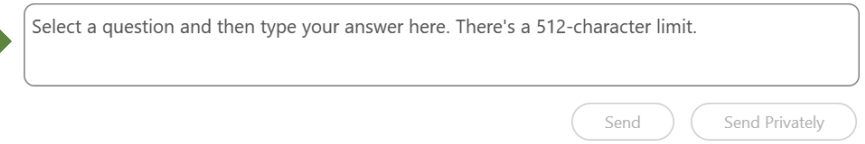

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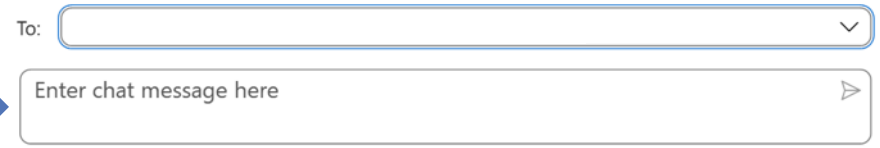

Q&A →

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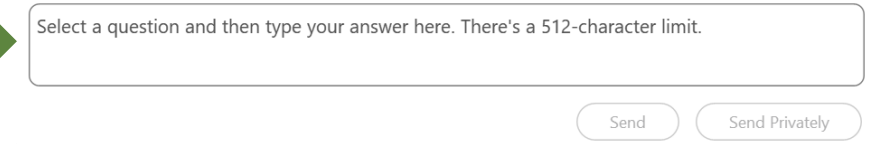

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Within a few days following today's event, visit

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WEBINAR 1: Demystifying Alzheimer's Blood Biomarkers: What Every Clinician Needs to Know

Live Event: Tuesday, December 9, 2025 | 1:00 pm – 2:00 pm EST

P.A.C.E.® Credit available until June 9, 2026 | Florida Lab Credit available

Recording

Slides

This foundational webinar will clarify the science and clinical role of blood-based biomarkers (BBMs) in Alzheimer's disease (AD). Analytical and clinical performance of AD BBM tests and appropriate positioning of testing within recommended diagnostic pathways alongside cognitive assessment, rule-out labs, and other testing modalities (PET/CSF) will be discussed. Special emphasis will be placed on interpreting positive, indeterminate, and negative test results. Included is a case-based dialogue to address common myths, patient communication tips, and how BBMs enable earlier access to specialist care and potential disease-modifying therapies.

Objectives:

- Differentiate AD BBM tests and key performance characteristics for amyloid pathology detection.
- Identify appropriate clinical use scenarios to order AD BBM tests within a structured diagnostic workup.
- Compare AD BBM tests to PET and CSF for amyloid/tau confirmation.
- Interpret positive, negative and indeterminate test results to guide patient management and patient/caregiver consultations.

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Dr. David Greeley is a Clinical Associate Professor in Neurology at the University of Washington School of Medicine. He has over 30 years of experience in clinical practice and research including in Alzheimer's disease and dementia. He worked as a neurologist and director of clinical research for a multi-specialty clinic in Spokane, Washington, and later founded Northwest Neurological, one of a few private practice neurologists in the region. Dr. Greeley is a Fellow in the American Academy of Neurology and an educator and trainer. He enjoys working in the yard, playing golf and pickleball with his wife and/or three daughters of whom he and his wife are most proud.

Disclosures

Receiving speaker honorarium from the program series sponsor, Fujirebio.

Former scientific advisor for AriBio.

Zivjena Vucetic, MD, PhD

Adjunct Assistant Professor

College of Science & Technology, Department of Biology

Temple University

Dr. Zivjena Vucetic is a physician-scientist with 20+ years of experience spanning clinical development, regulatory strategy and accelerating research and clinical use of immunoassays, epigenetic liquid-biopsy tests and metagenomic sequencing platforms. Dr. Vucetic holds a PhD in Biochemistry from Temple University School of Medicine, a Post-Doctoral Fellowship in Translational Medicine at the University of Pennsylvania and MD from the University of Zagreb. She is an Adjunct Assistant Professor at Temple University and has authored numerous peer-reviewed publications. Her passions include translating complex scientific innovations into scalable, clinically impactful solutions.

Disclosures

Receiving speaker honorarium from the program series sponsor, Fujirebio.

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Learning objectives

- Differentiate AD BBM tests and key performance characteristics for amyloid pathology detection.
- Identify appropriate clinical use scenarios to order AD BBM tests within a structured diagnostic workup.
- Compare AD BBM tests to PET and CSF for amyloid pathology confirmation.
- Interpret positive, negative and indeterminate test results to guide patient management and patient/caregiver consultations.

Poll #1

Describe your primary interest or use of biomarkers for cognitive decline.

a. To determine if the patient is POS or NEG for amyloid pathology
b. Use to refer patients to a specialist
c. Evaluate patients for anti-amyloid treatment
d. Track progression of patient's symptoms over time
e. General interest in learning more for clinical use
f. Research
g. Individual/personal reasons

The Foundation

Alzheimer's Disease Diagnosis and Blood Test Landscape

Alzheimer's disease diagnosis, treatment, and care guidelines have been evolving rapidly

Recent advances in 2025

- 1st FDA clearance for a blood biomarker (BBM) test to identify patients with amyloid pathology associated with Alzheimer's disease in specialized care setting
- 1st clinical practice guidelines for BBM use
- 2nd FDA clearance for a BBM test to aid in the initial assessment for Alzheimer's disease and other causes of cognitive decline

Dr. Alois Alzheimer first discovers AD[1]

Disease-modifying therapies (DMTs) become available

- FDA accelerated approval of 1st DMT aducanumab (Aduhelm)[8] — *Discontinued in 2024*[9]
- FDA approval of DMT lecanemab (Leqembi)[11]
- FDA approval of DMT donanemab (Kisunla)[12]

Changes in guidelines

- New guidelines proposed by the IWG for AD diagnostic criteria[4]
- NIA-AA research criteria for AD guidelines updated to include CSF markers[5]
- CSF biomarkers part of the NIA-AA biological definition of AD[6]
- Updated IWG guidelines: biomarkers *and* symptoms necessary for AD diagnosis[7]
- Updated IWG clinical-biological definition of AD: biomarker positive = "at risk" of AD[13]
- AA guidelines for the use of BBMs in clinical care published[14]

Detection of AD pathology

- Braak staging for tau tangles first published[2]
- Amyloid PET first performed in living humans[3]
- Preclinical AD characterized[5]
- 1st FDA-authorized CSF β-amyloid ratio (Aβ42/Aβ40) test for assessing early AD[10]
- 1st FDA-cleared pTau 217/Aß42 plasma test for assessing early AD pathology[15], pTau 181 initial assessment of AD

1906 · 1991 · 2004 · 2007 · 2011 · 2018 · 2021 · 2022 · 2023 · 2024 · 2025

AA, Alzheimer's Association; AD, Alzheimer's disease; BBM, blood biomarker; CSF, cerebrospinal fluid; DMT, disease-modifying therapy; FDA, United States Food and Drug Administration; IWG, international working group; NIA-AA, National Institute on Aging and Alzheimer's Association; pTau, phosphorylated tau; PET, positron emission tomography.

1. Hippius H, Neundörfer G. Dialogues Clin Neurosci. 2003;5(1):101–108. 2. Braak H, Braak E. Acta Neuropathol. 1991;82(4):239–259. 3. Klunk WE et al. Ann Neurol. 2004;55(3):306–319. 4. Dubois B et al. Lancet. 2007;6(8):734–746. 5. Sperling RA et al. Alzheimers Dement. 2011;7(3): 280–292. 6. Jack CR Jr et al. Alzheimers Dement. 2018;14(4):535–562. 7. Dubois B et al. Lancet Neurol. 2021;20(6):484–496. 8. Alexander GC et al. N Engl J Med. 2021;385(9):769–771. 9. Alzheimer's Association. Aducanumab to discontinued as Alzheimer's treatment. https://www.alz.org/alzheimers-dementia/treatments/aducanumab. Accessed September 4, 2025. 10. Medscape. FDA clears diagnostic test for early Alzheimer's. May 4, 2022. https://www.medscape.com/viewarticle/973451. Accessed September 4, 2025. 11. United States Food and Drug Administration. Press release. FDA converts novel Alzheimer's disease treatment to traditional approval. July 6 ,2023. https://www.fda.gov/news-events/press-announcements/fda-converts-novel-alzheimers-disease-treatment-traditional-approval. Accessed September 4, 2025. 12. United States Food and Drug Administration. Press release. FDA approves treatment for adults with Alzheimer's disease. July 2, 2024. https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-treatment-adults-alzheimers-disease. Accessed September 4, 2025. 13. Dubois B et al. JAMA Neurol. 2024;81(12):1304–1311. 14. Palmqvist S et al. Alzheimer's Dement. 2025;21(7):e70535.15. United States Food and Drug Administration. Press release. FDA clears first blood test used in diagnosing Alzheimer's disease. May 16, 2025. https://www.fda.gov/news-events/press-announcements/fda-clears-first-blood-test-used-diagnosing-alzheimers-disease. Accessed September 4, 2025.

Poll #1 - Results

Describe your primary interest or use of biomarkers for cognitive decline.

a. To determine if the patient is POS or NEG for amyloid pathology
b. Use to refer patients to a specialist
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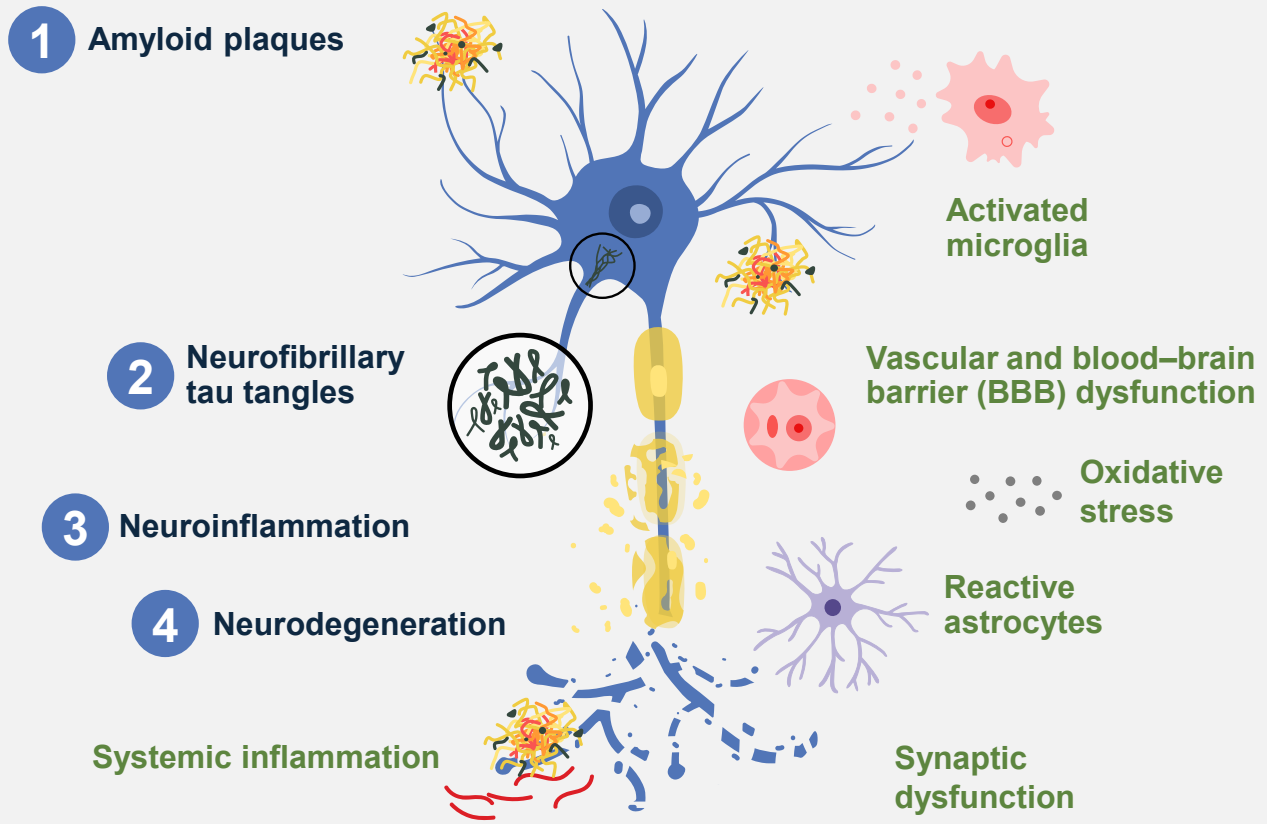
Overview

Alzheimer's Disease Pathophysiology

Alzheimer’s disease is a multifactorial, clinically heterogeneous neurodegenerative disorder[1-6]

Four cornerstone pathophysiological components of AD:

1. **Amyloid:** Amyloid-beta (Aβ) peptides accumulate in extracellular plaques, causing synaptic dysfunction
2. **Tau:** Abnormal tau proteins aggregate into intracellular tangles, interfering with neuronal structure and function
3. **Neuroinflammation:** Characterized by overactivated microglia and astrocytic reactivity
4. **Neurodegeneration:** Synaptic loss, neuronal death, and brain atrophy



Each process is linked to measurable biomarkers, including established and emerging markers[1,2]

Aβ, amyloid beta; AD, Alzheimer’s disease; BBB, blood–brain barrier.

1. Hung SY, Fu WM. J Biomed Sci. 2017;24(47):1–12. 2. Alzheimer’s Association. Alzheimers Dement. 2025;21(5):e70235. 3. Kinney JW et al. Alzheimers Dement. 2018;4:575–590. 4. Minter MR et al. J Neurochem. 2016;136(3):457–474. 5. Djurovic-Topalovic A et al. Am J Pathol. 2025;S0002-9440(25)00206-8. 6. Aisen PS et al. Alzheimers Res Ther. 2017;9(1):60.

Categorization of fluid and imaging biomarkers

Biomarker category	CSF or plasma analytes	Imaging
Core Biomarkers		
Core 1		
A (Aβ proteinopathy)	Aβ42	Amyloid PET
T_1: (phosphorylated and secreted AD tau)	p-tau217, p-tau181, p-tau231	
Core 2		
T_2 (AD tau proteinopathy)	MTBR-tau243, other phosphorylated tau forms (e.g., p-tau205), non-phosphorylated mid-region tau fragments[a]	Tau PET
Biomarkers of non-specific processes involved in AD pathophysiology		
N (injury, dysfunction, or degeneration of neuropil)	NfL	Anatomic MRI, FDG PET
I (inflammation) Astrocytic activation	GFAP	
Biomarkers of non-AD copathology		
V vascular brain injury		Infarction on MRI or CT, WMH
S α-synuclein	αSyn-SAA[a]	

1. Jack CR et al. Alzheimers Dement. 2024; 1-27.

Poll #2

If not applicable, please skip this question.

Which blood-based biomarkers do you currently order or offer to assess cognitive decline associated with AD: (Select all that apply.)

- Not sure of the specific marker(s)
- pTau 217
- pTau 181
- AD2 Algorithm
- Aβ42/40 ratio
- ApoE4
- pTau 217/Aβ42 ratio
- Other biomarkers

Understanding the Science

What Blood-based Biomarkers Measure in Alzheimer's Disease

Amyloid-beta plaques are primarily driven by Aβ42 aggregation[1] and have been visualized and quantified using Amyloid PET imaging for 20 years[2]

Aβ has two major isoforms

Aβ42	Aβ40
Main component of plaques; highly hydrophobic, aggregates easily[4]	Most abundant, less cytotoxic, can inhibit Aβ42 aggregation[4,5]

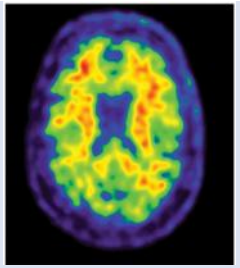
- Abnormal aggregation promotes accumulation of toxic Aβ oligomers, causing synaptic dysfunction and cognitive decline[3]

Aβ levels start to change early in the AD disease course[4]:

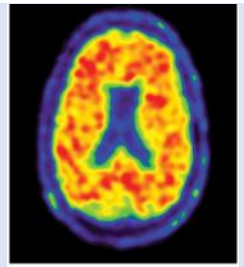
- Incorporating Aβ40 into the cerebrospinal fluid (CSF) Aβ42/40 ratio normalizes for overall amyloid production, which reduces interindividual variability and enhances diagnostic accuracy[4]

Lower Aβ42/Aβ40 ratio is associated with increased risk of cognitive decline and disease progression[4]

Amyloid-PET[7]



Healthy control



Patient with AD

- Amyloid PET is a noninvasive way to image amyloid plaques using labelled radiotracers[1]
- Where available, amyloid PET can be used clinically to aid in the early diagnosis of AD[7]

Amyloid PET application in AD

- Can define the total load and spatial distribution of Aβ pathology[7,8]
- Can identify underlying cerebral β-amyloidosis years before the onset of symptoms[8,9]

Aβ, amyloid-β; AD, Alzheimer's disease; APP, amyloid precursor protein; CSF, cerebrospinal fluid, PET, positron emission tomography.

1. Azargoonjahromi A. Mol Brain. 2024;17(44):1–24. 2. Chapleau M et al. J Nucl Med. 2022;63:13S–19S. 3. Alzheimer's Association. Alzheimers Dement. 2025;21(5):e70235. 4. Wang S et al. Front Aging Neurosci. 2024;16:1380237. 5. Jan A et al. J Biol Chem. 2008;283(42):281776–28189. 6. Kate MT et al. Alzheimers Res Ther. 2018;10:112. 7. Palmqvist S et al. Neurology. 2015;85(14):1240–1249. 8. Varghese T et al. Neurol Asia. 2013;18(3):239–248. 9. Johnson KA et al. Cold Spring Harb Perspect Med. 2012;2(4):a006213.

Poll #2 - Results

If not applicable, please skip this question.

Which blood-based biomarkers do you currently order or offer to assess cognitive decline associated with AD: (Select all that apply.)

- Not sure of the specific marker(s)
- pTau 217
- pTau 181
- AD2 Algorithm
- Aβmyloid 42/40 ratio
- ApoE4
- pTau 217/Aβ42 ratio
- Other biomarkers

Plasma amyloid biomarkers are associated with amyloid accumulation in brain across the AD spectrum

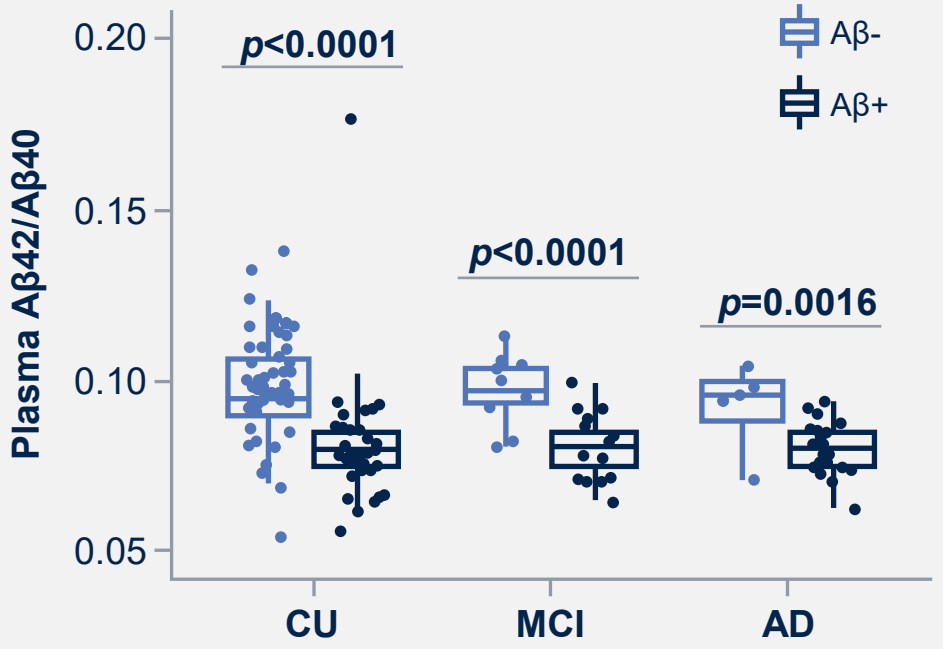
Plasma Aβ42 and the Aβ42/Aβ40 ratio

- Lower levels of **Aβ42** and a **lower Aβ42/Aβ40 ratio** reflect amyloid deposition in the brain[1]
- **Aβ42/Aβ40 ratio** normalizes to individual variation in Aβ levels[1]
- Plasma Aβ42/Aβ40 is associated with impaired function and cognition[2]
- Abnormal plasma Aβ42/Aβ40 remains low and stable over time, is enduring, and predicts accelerated cognitive decline[2]

Limitations of Aβ as stand-alone biomarker

- Aβ42/Aβ40 ratios in plasma have a smaller relative change compared to those in CSF to indicate positive amyloid PET[3]
- Peripheral production of Aβ (e.g., platelets, muscle, vascular tissue) contributes to circulating Aβ, limiting brain specificity[3]
- The diagnostic accuracy of plasma Aβ can be decreased by delays in processing samples[4]

A lower plasma Aβ42/Aβ40 ratio correlates with positive amyloid PET and CSF across the cognitive spectrum of AD[2]



Adapted from Trelle et al. 2025.

Aβ, amyloid-beta; AD, Alzheimer's disease; CSF, cerebrospinal fluid; CU, cognitively unimpaired; MCI, mild cognitive impairment; PET, positron emission tomography.

1. Agnello L et al. Curr Issues Mol Biol. 2025;47(8):580. 2. Trelle AN et al. Alzheimers Dement. 2025;21(2):e14442. 3. Zetterberg H, Blennow K. Mol Neurodegener. 2021;16(1):10. 4. Winston CN et al. J Alzheimers Dis. 2023;92(1):95-107.

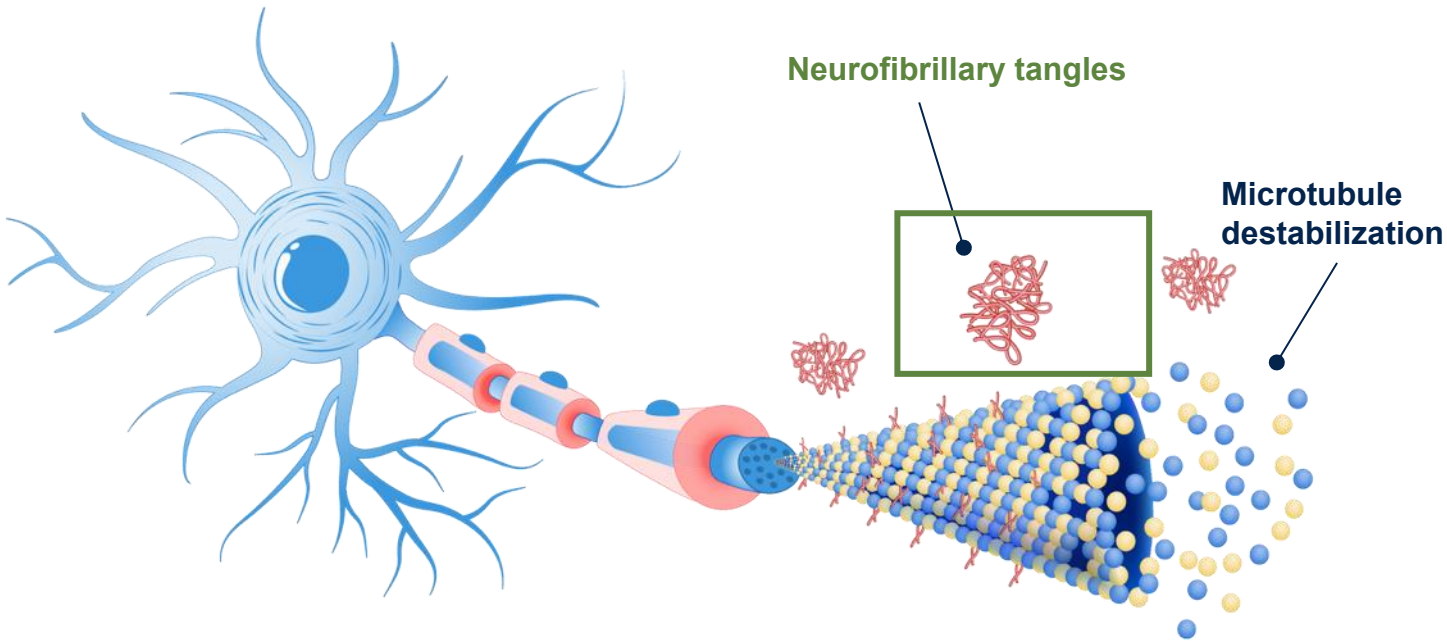
Tau tangles form when tau proteins are hyperphosphorylated, detach from microtubules, and aggregate[1,2]

Tau is a neuronal protein that **stabilizes microtubules and helps maintain cellular structure and transport[3]**

- Tau is abnormally phosphorylated in AD, causing it to detach from and destabilize microtubules[3]

Phosphorylated tau (pTau)[3]:

- Forms intracellular neurofibrillary tangles
- Correlates with cognitive decline and disease severity



Phosphorylation can occur at different sites on tau proteins, with isoform levels reflecting disease progression[3]
Early-changing tau biomarkers correlate with amyloid pathology while late-changing tau biomarkers are related to neurofibrillary tangle load[4]

AD, Alzheimer's disease; pTau, phosphorylated tau.

1. Hung SY, Fu WM. J Biomed Sci. 2017;24(47):1–12. 2. Alzheimer's Association. Alzheimers Dement. 2020;16:391–460. 3. Rawat P et al. Int J Mol Sci. 2022;23(21):12841. 4. Hampel H et al. Neuron. 2023;111(18):2781–2799.

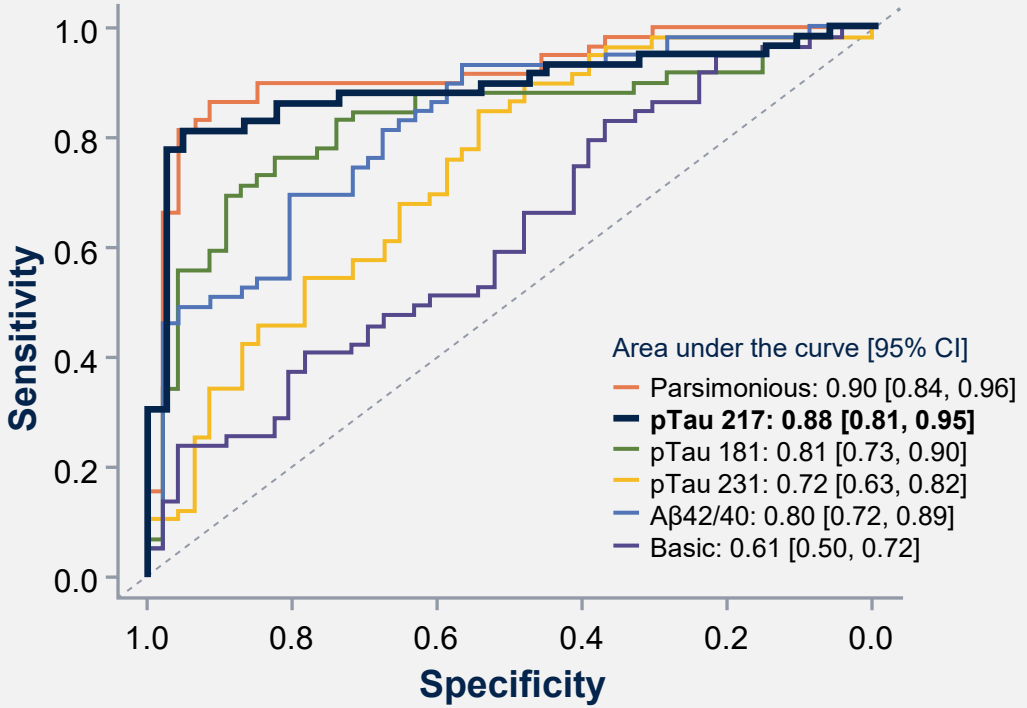
Tau blood biomarkers: plasma pTau 217 is an effective biomarker of Alzheimer's disease pathophysiology[1]

Plasma pTau 217

- Shows strong agreement with both CSF amyloid biomarkers and PET imaging[1,2]
- Detects amyloid and tau pathology[1,2]
- Helps distinguish AD from other neurodegenerative diseases[2]
- Has better diagnostic accuracy than Aβ42/40 in identifying AD pathology and predicting disease progression[3-5]

Longitudinal increases in plasma pTau 217 correlate with worsening cognition, greater amyloid burden, and higher likelihood of progression from MCI to AD dementia[6,7]

pTau 217 outperforms other pTau isoforms in predicting AD pathology[3-5]

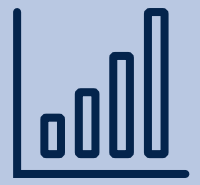


Adapted from Salvadó G et al. 2023. Associations between multiple plasma biomarkers (antemortem) and neuropathological data (postmortem) were assessed for 105 individuals in the AZSAND cohort (Arizona Study of Aging and Neurdegenerative Disorders).

Aβ, amyloid-beta; AD, Alzheimer's disease; CI, confidence interval; CSF, cerebrospinal fluid; MCI, mild cognitive impairment; PET, positron emission tomography; pTau, phosphorylated tau.

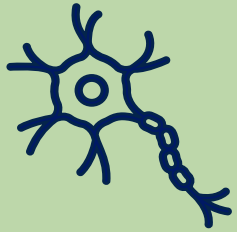
1. Khalafi M et al. Alzheimers Dement. 2025;21(2):e14458. 2. Palmqvist S et al. JAMA. 2020;324(8):772-781. 3. Janelidze S et al. Nat Commun. 2020;11(1):1683. 4. Schöll M et al. J Prev Alzheimers Dis. 2025;12(4):100056. 5. Salvadó G et al. EMBO Mol Med. 2023;15(5):e17123. 6. Mattsson-Carlgren N et al. Brain. 2020;143(11):3234-3241. 7. Groot C et al. Alzheimers Res Ther. 2022;14(1):67. 8. Lehmann S et al. eBioMedicine 2025;117: 105805. 9. Arranz J et al. Alzheimers Res Ther. 2024;16(1):139.

Composite biomarker advantages over single analytes



Composite biomarkers have **higher diagnostic accuracy** than single-analyte markers[1,2]

E.g., pTau 217/Aβ42 vs pTau 217 alone



Hybrid markers can **represent more than one aspect** of disease pathology and can integrate signals from distinct but related processes[3]

E.g., amyloid-tau ratios

Normalizing ratios help **control for differences** in overall protein production and inter-individual variability[4]

E.g., Aβ42/Aβ40 normalizes Aβ42 levels to total Aβ production[5]

- Improves correlation with amyloid PET and CSF tests
- Reduces false positives seen with Aβ42 alone

Aβ, amyloid-beta; AD, Alzheimer's disease; CSF, cerebrospinal fluid; PET, positron emission tomography.

1. Cullen NC et al. Nat Commun. 2021;12(1):3555. 2. Wang J et al. Alzheimers Dement. 2025;21(3):e70038. 3. Li Y et al. Ann Neurol. 2024;95(5):951-965. 4. Janelidze S et al. Ann Clin Transl Neurol. 2016;3(3):154-165. 5. Schöll M et al. J Prev Alzheimers Dis. 2025;12(4):100056.

Tau/Amyloid composite blood biomarkers: the pTau 217/Aβ42 ratio enhances diagnostic performance when compared to individual biomarkers[1-3]

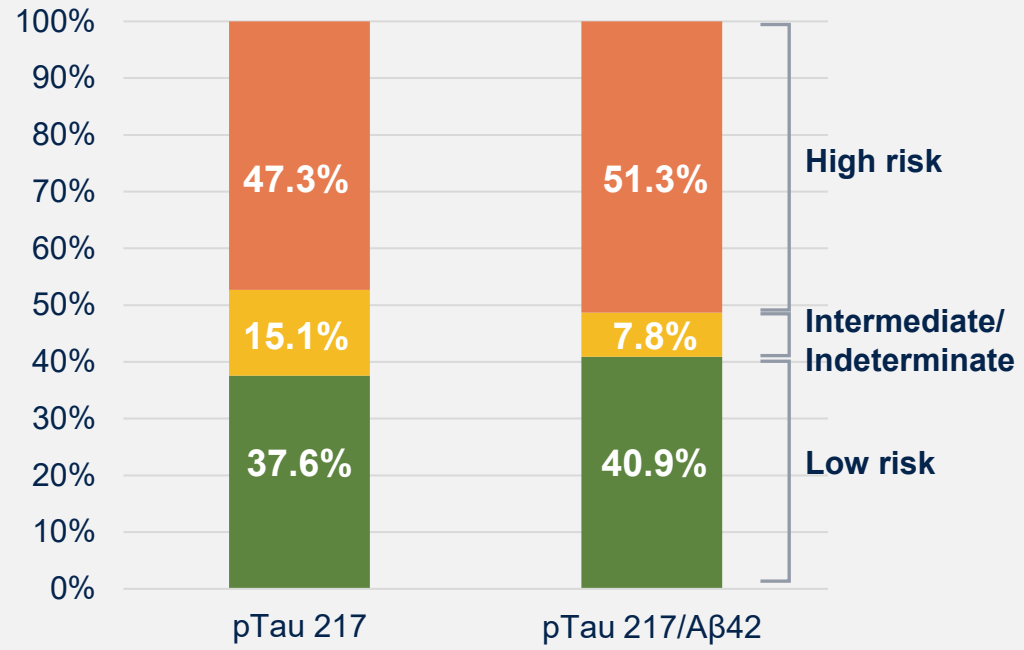
Plasma pTau 217/Aβ42

- High concordance with PET and CSF biomarkers[4,5]
- The added diagnostic value is most apparent in early-stage AD, when amyloid prevalence is low.[2]

Common medical conditions (i.e, diabetes and cardiovascular disease) may obscure the association between BBMs and Aβ[1]

- **pTau 217/Aβ42** ratio may mitigate the effect of some comorbidities on diagnostic accuracy compared to pTau 217 alone[1]

pTau 217/Aβ42 ratio reduced the number of tests that return an "intermediate/indeterminate" result for patients with cognitive complaints consistent with early AD[2-4]



Adapted from Lehmann S et al. 2025.
Cut-offs selected on 90% sensitivity and specificity and tested in the prospective ALZAN cohort.

Aβ, amyloid-beta; AD, Alzheimer's disease; BBM, blood biomarker; CSF, cerebrospinal fluid; PET, positron emission tomography; pTau, phosphorylated tau.

1. Olvera-Rojas M et al. Alzheimers Dement. 2024;21(2):e14430. 2. Wang J et al. Alzheimers Dement. 2025;21(3):e70038. 3. Martínez-Dubarbie F et al. Alzheimers Res Ther. 2025;17(68):1–16. 4. Lehmann S et al. eBiomedicine. 2025;117:105805. 5. Palmqvist S et al. Neurology. 2015;85:1240–1249-.

Performance Parameters

The Clinical Relevance

Understanding the statistics associated with biomarker tests can help decipher their clinical relevance[1,2]

Sensitivity and specificity represent probability of the test correctly identifying the known disease state

Sensitivity
A test's ability to correctly detect individuals who have the condition (% accurate true positives)

Specificity
A test's ability to correctly reject healthy individuals without a condition (% accurate true negatives)

Test result	Known **disease state** +	Known **disease state** −
+	True positive	False positive
−	False negative	True negative

All potential combinations of test results and disease states.

Assessing the test accuracy given the known disease state

$$\textbf{Sensitivity} = \frac{\text{true positives}}{\text{true positives + false negatives}}$$

$$\textbf{Specificity} = \frac{\text{true negatives}}{\text{true negatives + false positives}}$$

At **90%** sensitivity:

- 90/100 people with AD pathology are identified by the test (true positives)
- 10 will be missed (false negatives)

At **90%** specificity:

- 90/100 people without AD pathology identified by the test (true negatives)
- 10 incorrectly identified as having AD (false positives)

AD, Alzheimer's disease.

1. Wang H et al. Gen Psychiatr. 2021;34(2):e100453. 2. Trevethan R. Front Public Health. 2017;5:307.

Understanding the statistics associated with biomarker tests can help decipher their clinical relevance[1,2]

Sensitivity and specificity represent probability of the test correctly identifying the known disease state

Sensitivity
A test's ability to correctly detect individuals who have the condition (% accurate true positives)

Specificity
A test's ability to correctly reject healthy individuals without a condition (% accurate true negatives)

Test result	Known **disease state** +	Known **disease state** −
+	True positive	False positive
−	False negative	True negative

All potential combinations of test results and disease states.

Assessing the test accuracy given the known disease state

$$\textbf{Sensitivity} = \frac{\text{true positives}}{\text{true positives + false negatives}}$$

$$\textbf{Specificity} = \frac{\text{true negatives}}{\text{true negatives + false positives}}$$

At **90%** sensitivity:

- 90/100 people with AD pathology are identified by the test (true positives)
- 10 will be missed (false negatives)

At **75%** specificity:

- 75/100 people without AD pathology identified by the test (true negatives)
- 25 incorrectly identified as having AD (false positives)

AD, Alzheimer's disease.

1. Wang H et al. Gen Psychiatr. 2021;34(2):e100453. 2. Trevethan R. Front Public Health. 2017;5:307.

Predictive values of a test will change based on the underlying prevalence of the condition[1,2]

Condition prevalence

50%

TEST

90% sensitivity

90% specificity

Given to 2 populations

Condition prevalence

10%

PPV
90%

Positive test:
90% probability that the individual has the condition

NPV
90%

Negative test:
90% probability that the individual truly does not have the condition

Clinical relevance:

The same test will perform differently in different clinical settings

(e.g., memory clinics vs. general screening for AD)

PPV
50%

Positive test:
50% probability that the individual has the condition

NPV
98.7%

Negative test:
98.7% probability that the individual truly does not have the condition

AD, Alzheimer's disease; NPV, negative predictive value; PPV, positive predictive value.

1. Wang H et al. Gen Psychiatr. 2021;34(2):e100453. 2. Trevethan R. Front Public Health. 2017;5:307.

Predictive values of a test will change based on the underlying prevalence of the condition[1,2]

Condition prevalence

50%

TEST

90% sensitivity

75% specificity

Given to 2 populations

Condition prevalence

10%

PPV
78%

Positive test:
78% probability that the individual has the condition

NPV
88%

Negative test:
88% probability that the individual truly does not have the condition

Clinical relevance:

The same test will perform differently in different clinical settings

(e.g., memory clinics vs. general screening for AD)

PPV
29%

Positive test:
29% probability that the individual has the condition

NPV
98.5%

Negative test:
98.5% probability that the individual truly does not have the condition

AD, Alzheimer's disease; NPV, negative predictive value; PPV, positive predictive value.

1. Wang H et al. Gen Psychiatr. 2021;34(2):e100453. 2. Trevethan R. Front Public Health. 2017;5:307.

Summary of FDA-approved tracers and FDA-cleared assay performance characteristics

FDA-approved tracers and FDA-cleared assays	Sensitivity *mean (95% CI)*	Specificity *mean (95% CI)*	NPV *mean (95% CI)*	PPV *mean (95% CI)*	AD pathology presence (%) in test population	AD pathology confirmation method(s)
Amyloid PET tracers						
Florbetapir[1]	**92%** (78%, 98%)	**100%** (80%, 100%)	*unpublished*	*unpublished*	*unpublished*	Postmortem neuropathology
Flutemetamol[2]	**93%** (81%, 99%)	**84%** (64%, 96%)	*unpublished*	*unpublished*	*unpublished*	Postmortem neuropathology
Florbetaben[3]	**96.2%** (86.8%, 99.5%)	**80%** (61.4%, 92.3%)	*unpublished*	*unpublished*	*unpublished*	Postmortem neuropathology
CSF biomarkers						
Aβ42/Aβ40 ratio[4]	*unpublished*	*unpublished*	**83.9%** (75.1%, 90.0%)	**96.6%** (92.8%, 98.4%)	68.2%	Amyloid PET scan results
pTau 181/Aβ42 ratio[5]	*unpublished*	*unpublished*	**87.1%** (83.5%, 90.0%)	**93.3%** (90.3%, 95.4%)	53.7%	Amyloid PET scan results
t-tau 181/Aβ42 ratio[6]	*unpublished*	*unpublished*	**84.4%** (80.8%, 87.4%)	**94.2%** (91.3%, 96.3%)	53.7%	Amyloid PET scan results
Blood biomarkers						
pTau 217/Aβ42 ratio	**97.6%**[7] *(CI unavailable)*	**90.8%**[7] *(CI unavailable)*	**97.3%** (93.9%, 98.8%)[8]	**91.8%** (87.8, 94.6%)[8]	51.1%[8]	Positive amyloid PET and/or amyloid CSF ratio[8]
pTau 181	*92.7% (80.6%, 97.5%)*[9]	*51.3% (45.4%, 57.2%)*[9]	97.9% (94.5%, 99.3%)[9]	22.4% (19.5%, 25.0%)[9]	13.1%[9]	Visual Amyloid PET Read

Predictive values of pTau 217/Aβ 42 ratio are similar to those of CSF tests. pTau 181 offers similar NPV but very low PPV compared to CSF.

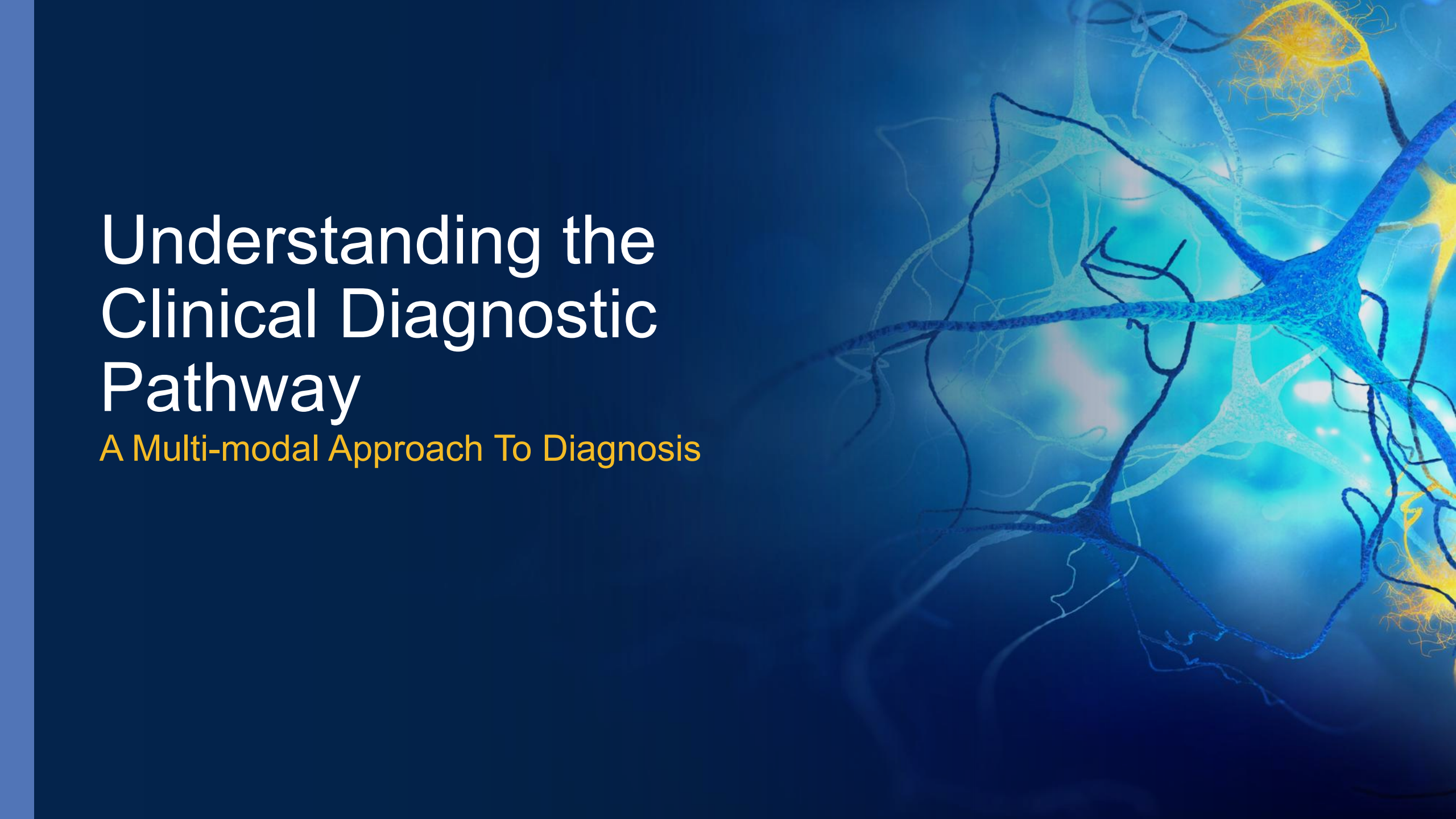
Caveat: These were not head-to-head comparisons. The performance characteristics are based on different populations in different settings and cannot be directly compared.

Aβ, amyloid-beta; AD, Alzheimer's disease; CI, confidence interval; CSF, cerebrospinal fluid; FDA, United States Food and Drug Administration; NPV, negative predictive value; PET, positron emission tomography; PPV, positive predictive value; pTau, phosphorylated tau; t-tau, total tau.

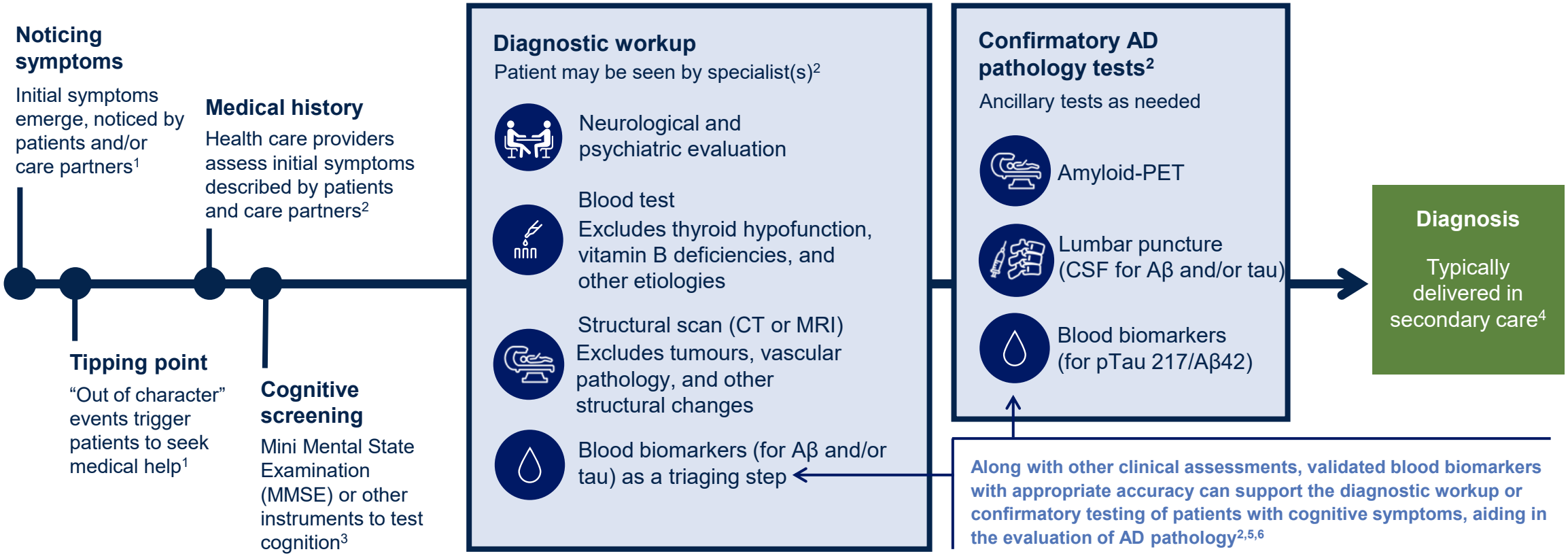
1. Amyvid® (florbetapir F 18 injection). Prescribing information. Eli Lilly and Company. Revised 06/2025. 2. Vizamyl™ (flutemetamol F 18 injetion). Prescribing information. GE Healthcare. Updated 06/2025. 3. Neuraceq® (florbetaben F 18 injection). Prescribing information. Life Molecular Imaging. Revised 06/2025. 4. FDA clearance summary. Lumipulse G ~-Amyloid Ratio (1-42/1-40). 5. FDA clearance summary. Roche Elecsys β-Amyloid (1-42) CSF II and Elecsys Phospho-Tau (181P) CSF. 6. FDA equivalence summary. Roche Elecsys β-Amyloid (1-42) CSF II and Elecsys Total-Tau CSF. 7. Global CEO Initiative. The Alzheimer's Blood Test Performance Database. Accessed September 11, 2025. https://alzdiagnostichub.org/blood-test-performance-database/ 8. Lumipulse G pTau217/ß-Amyloid 1-42 Plasma Ratio. Package insert. Fujirebio Diagnostics. 9. Elecsys Phospho-Tau (181P) Plasma. 510(k) Decision Summary K252163. Roche Diagnostics.

Understanding the Clinical Diagnostic Pathway

A Multi-modal Approach To Diagnosis



The introduction of blood biomarkers could support the current Alzheimer's disease diagnostic pathway as triaging or confirmatory tools



Note: The diagnostic pathway is not yet standardized, and implementation may be unique to each medical center[7]

Aβ, amyloid beta; AD, Alzheimer's disease; CSF, cerebrospinal fluid; CT, computed tomography; HCP, healthcare professional; MMSE, Mini Mental State Examination; MRI, magnetic resonance imaging; PET, positron emission tomography

1. The Alzheimer's Association. Special report. The patient journey in an era of new treatments. 2023. https://www.alz.org/getmedia/12127c15-bc6b-4410-b1ba-a6402cccfe17/alzheimers-facts-and-figures-special-report-2023.pdf. Accessed September 12, 2025. 2. Mielke MM et al. Alzheimers Dement. 2024;20:8216–8224. 3. Choe YM et al. Neuropsychiatr Dis Treat. 2020;16:1767–1775. 4. Dickerson BC. Alzheimers Dement. 2025;21:e14337. 5. Hampel H et al. Neuron. 2023;111(18):2781–2799. 6. Palmqvist S et al. Alzheimers Dement. 2025;21(7):e70535. 7. Snider, BJ et al. Alzheimers Dement Trans Res Clin Intervent. 2025;11:e70094.

Poll # 3

***If not clinically applicable to you**, please skip this question*

Do you incorporate the 2025 Alzheimer's Association's guidelines for use of blood-based biomarkers in your clinical practice?

- Routinely
- In select patients
- Never
- I don't yet know the guidelines

In July 2025, the Alzheimer's Association released the first guidelines for use of blood biomarkers in clinical practice[1]

In patients with **objective cognitive impairment** presenting to **specialized memory care,** minimum BBM test accuracies[a,b] are necessary for their use:

Scenario 1: BBM as a confirmatory test of AD

- Negative result rules out AD pathology with high probability
- Positive test confirms AD pathology with a high probability
- May serve as a reasonable substitute for CSF or amyloid PET confirmation

MINIMUM BBM TEST ACCURACY[a,b]:

≥90% High sensitivity

≥90% High specificity

Scenario 2: BBMs as a triaging test

- Negative result rules out AD pathology with a high probability
- A positive result may require confirmation via another method (e.g., CSF AD biomarkers or amyloid PET)

MINIMUM BBM TEST ACCURACY[a,b]:

≥90% High sensitivity

≥75% Specificity

[a]Compared against reference test (CSF AD biomarkers, amyloid PET, or AD neuropathology).
[b]Acceptable accuracy of tests were based on what clinicians in real-world setting would find acceptable; recent expert opinion was used as a starting point for this alignment.[2]
AD, Alzheimer's disease; BBM, blood biomarker; CSF, cerebrospinal fluid; PET, positron emission tomography.
1. Palmqvist S et al. Alzheimer's Dement. 2025;21(7):e70535. 2. Schindler SE et al. Nat Rev Neurol. 2024;20:426-439.

Poll # 3 - Results

***If not clinically applicable to you**, please skip this question*

Do you incorporate the 2025 Alzheimer's Association's guidelines for use of blood-based biomarkers in your clinical practice?

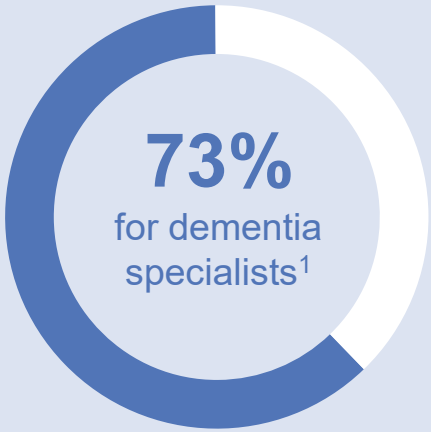
- Routinely
- In select patients
- Never
- I don't yet know the guidelines

What is the value in confirming amyloid in patients with cognitive impairment?

Diagnostic accuracy

For symptomatic patients, the accuracy of a clinical diagnosis can be suboptimal[1]

In one study, the accuracy of AD pathology detection without blood biomarkers was



Preventing treatment delays

Newer treatment options are approved for use in early AD. Delays in confirmation of amyloid may permit AD to progress and thereby limit treatment options[2]

Clinical trials

Most phase 3 clinical trials require evidence of amyloid positivity for trial inclusion[3]

Disease-modifying therapies

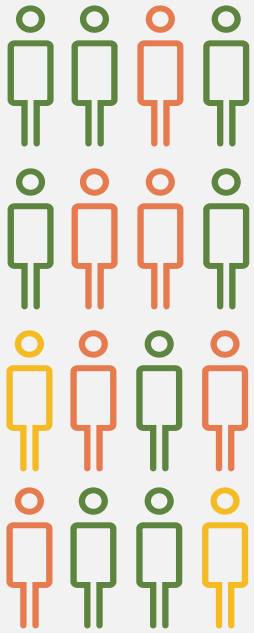
Initiating anti-amyloid immunotherapy requires biomarker-positive test results for AD[1]

AD, Alzheimer's disease.

1. Palmqvist S et al. JAMA. 2024;332(15):1245-1257. 2. Snider, BJ et al. Alzheimers Dement Trans Res Clin Intervent. 2025;11:e70094. 3. Cummings J et al. Alzheimer's Dement (NY). 2024;10(2):e12465.

A two-cut-off approach for blood biomarkers allows for confirmation and triaging in-and-out of patients with cognitive symptoms[1,2]

People with cognitive symptoms



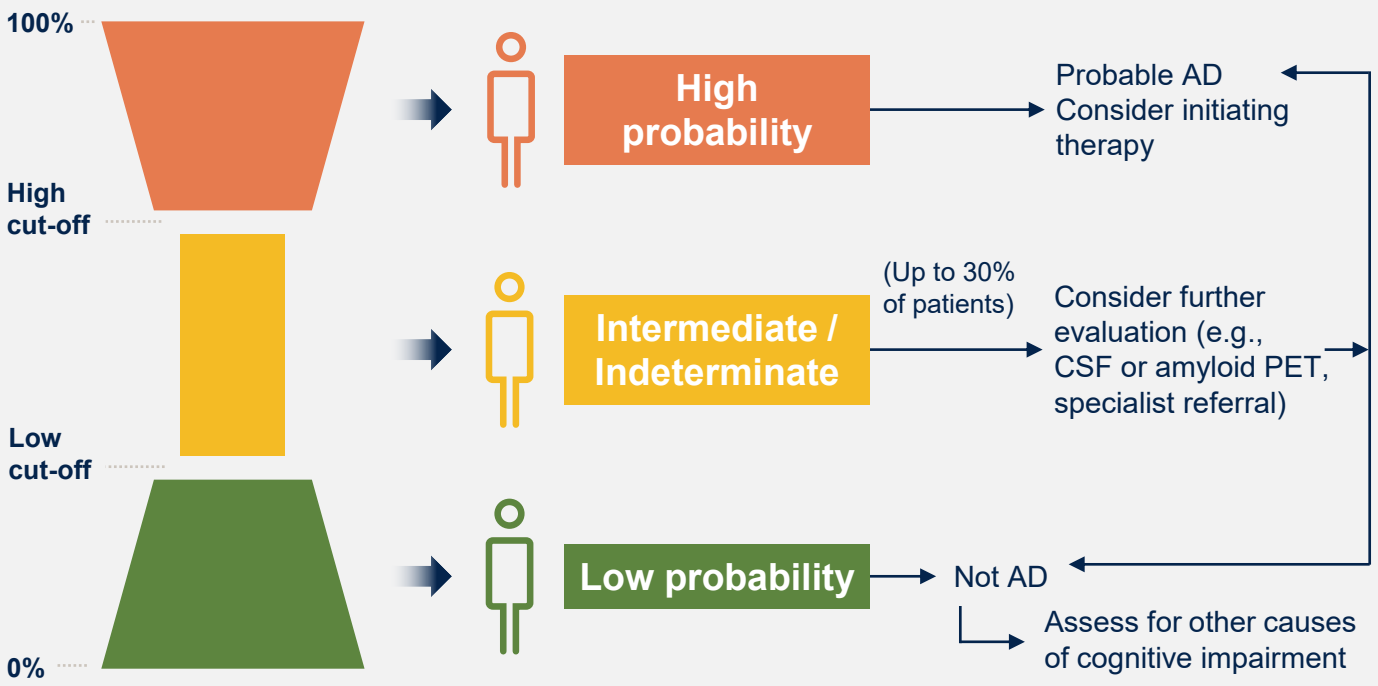
BBM testing

Optimal performance

≥90% High sensitivity

≥90% High specificity

Probability of amyloid PET positivity



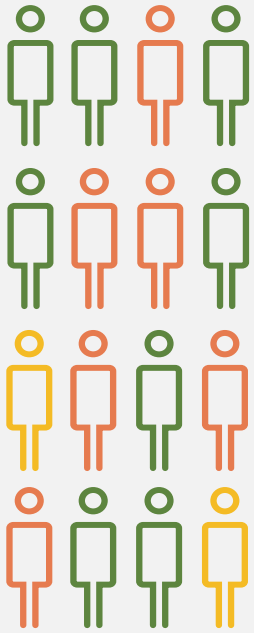
Using a BBM approach could allow for an 83% reduction in the need for CSF or PET imaging[3]

AD, Alzheimer's disease; BBM, blood biomarker; CSF, cerebrospinal fluid; PET, positron emission tomography.

1. Hansson O et al. Nat Aging. 2023;3(5):506–519. 2. Brum WS et al. Nat Aging. 2023;3(9):1079–1090. 3. Mattsson-Carlgren N et al. JAMA Neurol. 2024;81(1):69–78 4. Schindler SE et al. Nat Rev Neurol. 2024;20(7):426-439.

A single-cut-off approach for blood biomarkers allows for triaging-out patients with cognitive symptoms

People with cognitive symptoms



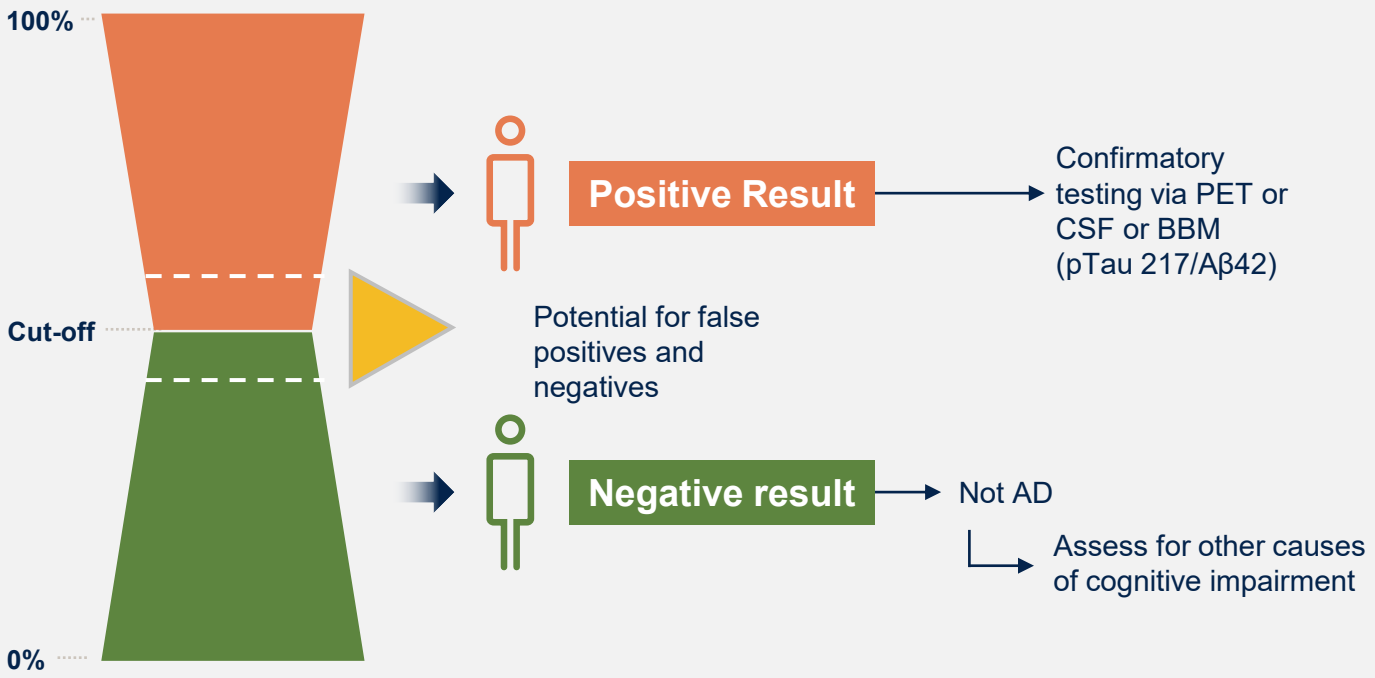
BBM testing

Acceptable performance

≥90% High sensitivity

≥75% Specificity

Probability of amyloid PET positivity



- Single cut-off approach benefits from a clear binary outcome. Positive or Negative.
- Challenge arises where there is overlap between test results in those with and without disease or overlap in the 95% CI for test positivity or negativity, leading to indeterminate results.[1]
- Single cutoff tests typically are used as a rule out test due to the lower PPV and higher NPV. Due to the lower predictive value of the positive result, a significantly large number of patients undergo confirmatory testing.

AD, Alzheimer's disease; BBM, blood biomarker; CSF, cerebrospinal fluid; PET, positron emission tomography.

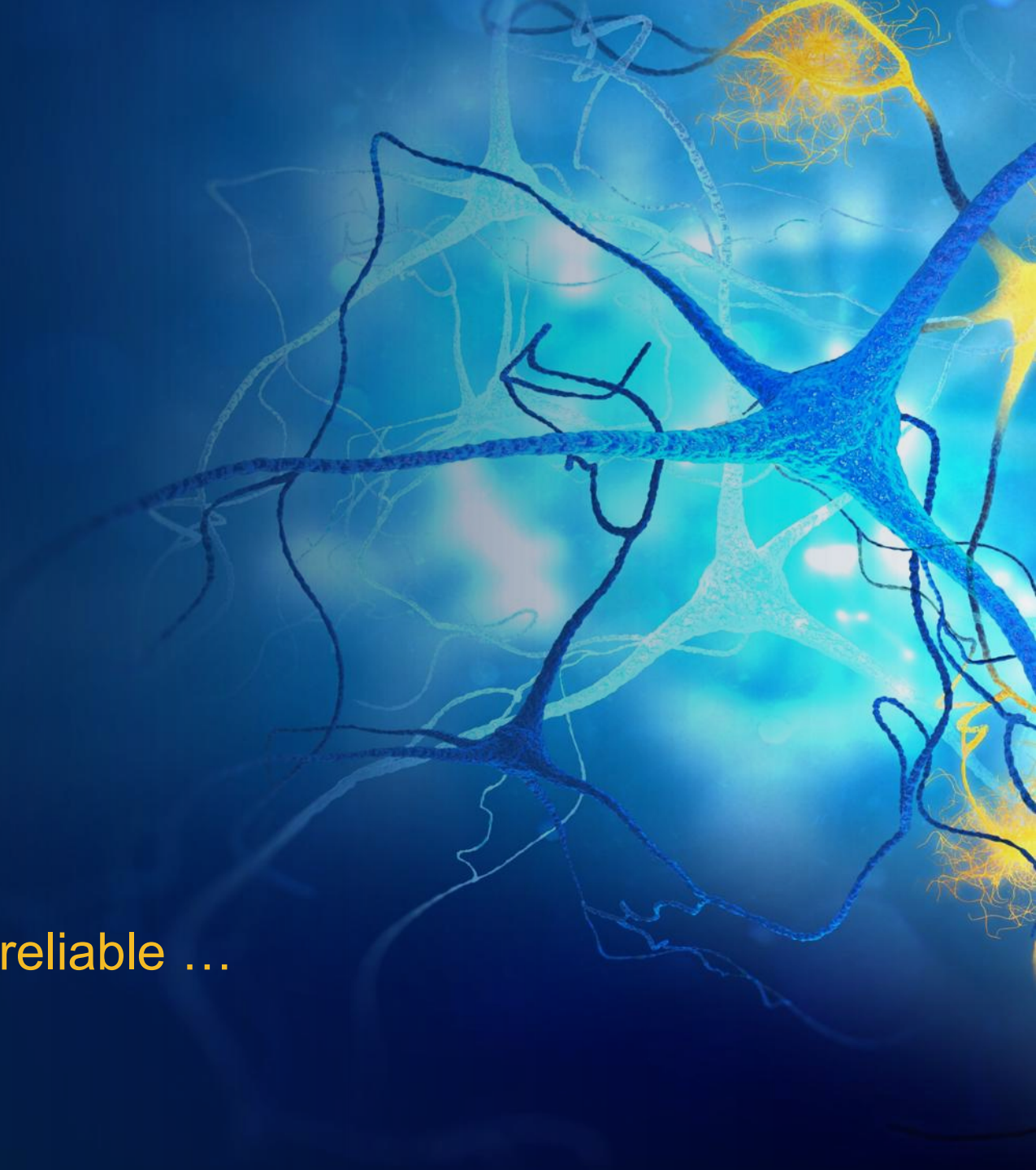
1. Hazan J et al. Alzheimer's & Dementia. 2025; 21:370113.

Myth-busting

BBMs are experimental…

BBMs are triaging tests…

Results aren’t sufficiently reliable …



pTau 217/Aβ42 Plasma Ratio demonstrated high predictive value in patients (aged 50+) with symptoms of cognitive decline

- The study patient population:
  - n=499, ages of 52 and 93 years
  - Patients presenting at specialized care setting with signs and symptoms of cognitive decline
  - Amyloid positivity confirmed by historic amyloid PET with an FDA-cleared tracer or FDA-cleared amyloid CSF ratio
- Diverse patient population from multiple cohorts
  - Polaris-AD, BioFINDER-2, Bio-Hermes-001, and WRAP

pTau 217 / Aβ42 Plasma Ratio

pTau 217 / Aβ42 Plasma Ratio	PET/CSF		Total (n)	Frequency (%) (95% CI)	Predictive value (PV)% (95% CI)	Likelihood Ratio (95% CI)
	Pos (n)	Neg (n)				
Positive	201	18	219	43.9%	91.8% (87.8%, 94.6%)	10.68 (6.90, 16.79)
Indeterminate	49	49	98	19.6%	50.0% (41.3%, 58.8%)	0.96 (0.67, 1.36)
Negative	5	177	182	36.5%	2.7% (1.2%, 6.1%)	0.03 (0.01, 0.06)
Total	255	244	499	**Prevalence=51.1%**		

Lumipulse G pTau217/ß-Amyloid 1-42 Plasma Ratio. Package insert. Fujirebio Diagnostics.

pTau 217/Aβ42 Plasma Ratio shows strong alignment with amyloid PET and CSF results

pTau 217 / Aβ42 Plasma Ratio: Visual Amyloid PET

pTau 217 / Aβ42 Plasma Ratio	PET		Total (n)	Frequency (%) (95% CI)	Predictive value (PV)% (95% CI)	Likelihood Ratio (95% CI)
	Pos (n)	Neg (n)				
Positive	56	6	62	40.8%	90.3% (81.8%, 95.3%)	12.16 (5.85, 26.37)
Indeterminate	9	20	29	19.1%	31.0% (18.0%, 47.3%)	0.59 (0.29, 1.17)
Negative	1	60	61	40.1%	1.6% (0.3%, 8.2%)	0.02 (0.00, 0.12)
Total	66	86	152	**Prevalence=43.4%**		

pTau 217 / Aβ42 Plasma Ratio: CSF

pTau 217 / Aβ42 Plasma Ratio	CSF		Total (n)	Frequency (%) (95% CI)	Predictive value (PV)% (95% CI)	Likelihood Ratio (95% CI)
	Pos (n)	Neg (n)				
Positive	145	12	157	45.2%	92.4% (87.8%, 95.4%)	10.10 (5.95, 17.54)
Indeterminate	40	29	69	19.9%	58.0% (47.5%, 67.9%)	1.15 (0.76, 1.77)
Negative	4	117	121	34.9%	3.3% (1.3%, 7.9%)	0.03 (0.01, 0.07)
Total	189	158	347	**Prevalence=54.5%**		

Lumipulse G pTau217/ß-Amyloid 1-42 Plasma Ratio. Package insert. Fujirebio Diagnostics.

pTau 217/Aβ42 Plasma Ratio shows strong positive predictive performance across the AD diagnostic categories

SCD

pTau 217 / Aβ42 Plasma Ratio	PET/CSF		Total (n)	Frequency (%) (95% CI)	Predictive value (PV)% (95% CI)	Likelihood Ratio (95% CI)
	Pos (n)	Neg (n)				
Positive	11	1	12	24.5%	91.7% (67.3%, 98.5%)	17.37 (3.29, 100.51)
Indeterminate	8	8	16	32.7%	50.0% (31.1%, 68.5%)	1.58 (0.71, 3.44)
Negative	0	21	21	42.9%	0.0% (0.0%, 13.3%)	0.00 (0.000, 0.243)
Total	19	30	49			

MCI

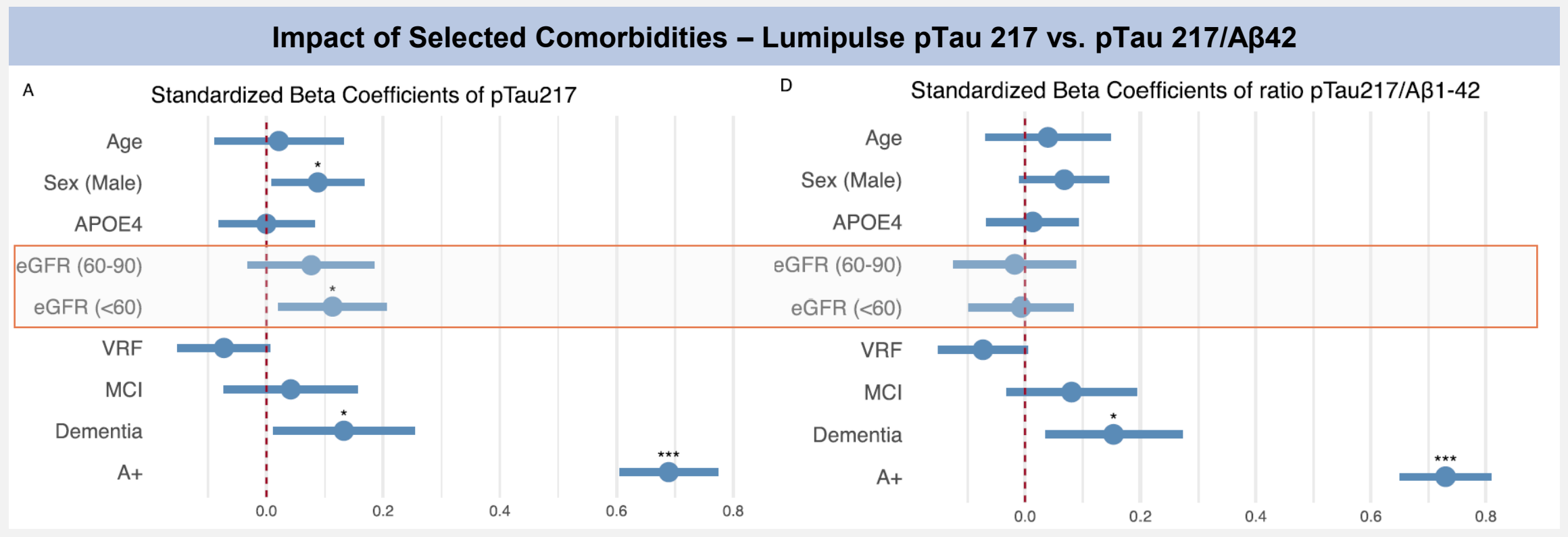
pTau 217 / Aβ42 Plasma Ratio	PET/CSF		Total (n)	Frequency (%) (95% CI)	Predictive value (PV)% (95% CI)	Likelihood Ratio (95% CI)
	Pos (n)	Neg (n)				
Positive	52	6	58	37.7%	89.7% (80.5%, 95.0%)	12.52 (5.99, 27.20)
Indeterminate	10	14	24	15.6%	41.7% (25.5%, 59.5%)	1.03 (0.49, 2.13)
Negative	1	71	72	46.8%	1.4% (0.2%, 7.0%)	0.02 (0.004, 0.109)
Total	63	91	154			

AD

pTau 217 / Aβ42 Plasma Ratio	PET/CSF		Total (n)	Frequency (%) (95% CI)	Predictive value (PV)% (95% CI)	Likelihood Ratio (95% CI)
	Pos (n)	Neg (n)				
Positive	136	11	147	50.7%	92.5% (87.8%, 95.6%)	8.73 (5.08, 15.48)
Indeterminate	30	27	57	19.7%	52.6% (41.3%, 63.9%)	0.78 (0.50, 1.25)
Negative	4	82	86	29.7%	4.7% (1.9%, 11.0%)	0.03 (0.01, 0.09)
Total	170	120	290			

Lumipulse G pTau217/ß-Amyloid 1-42 Plasma Ratio. Package insert. Fujirebio Diagnostics.

pTau 217/Aβ42 Plasma Ratio demonstrates resilience to comorbidities

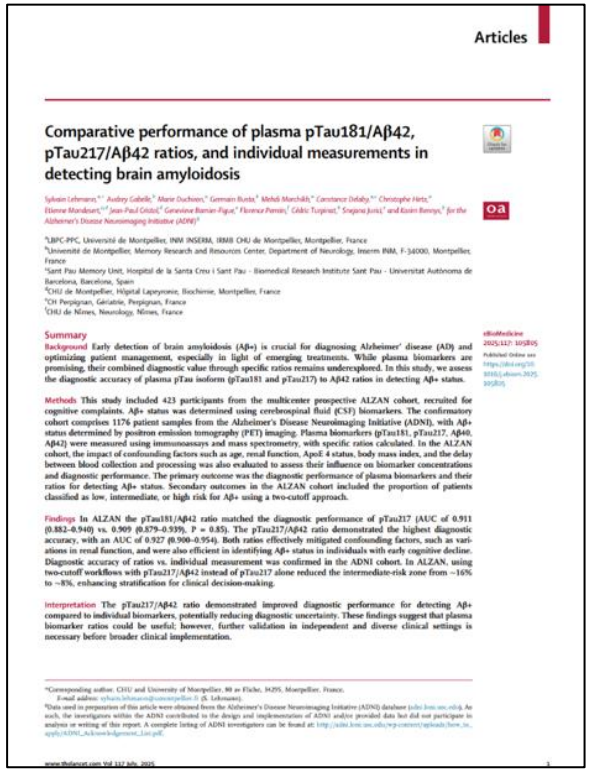


Arranz J, et al. [Preprint]. 2023 Dec doi: 10.21203/rs.3.rs-3725688/v1. Update in: Alzheimers Res Ther. 2024 Jun 26;16(1):139. doi: 10.1186/s13195-024-01513-9.

- Using the plasma pTau 217/Aβ42 ratio appears to mitigate the impact of comorbidities, including CKD
- Further studies are ongoing to evaluate the reliability of this ratio in individuals with comorbidities.

1. Palmqvist, S et al. Nat Med 2025. 2. Lehmann S et al. "medRxiv, My 30. 2025. doi: https://doi.org/10.1101/2024.12.07.24318640. 3. Arranz J et al. Alzheimers Res Ther. 2024 Jun 26;16(1):139.

Initial evaluations of the pTau 217/Aβ42 Plasma Ratio performance in primary care



Articles

Comparative performance of plasma pTau181/Aβ42, pTau217/Aβ42 ratios, and individual measurements in detecting brain amyloidosis

Sylvain Lehmann,[a,*] Audrey Gabelle,[b] Marie Duchiron,[a] Germain Rivata,[a] Mehdi Marchihi,[a] Constance Delaby,[a,c] Christophe Hirtz,[a] Etienne Mondesert,[a,d] Jean-Paul Cristol,[e] Geneviève Bernin-Figue,[a] Florence Pernin,[f] Cédric Turpinat,[a] Snejana Jurisic,[a] and Kasim Bennys,[a] for the Alzheimer's Disease Neuroimaging Initiative (ADNI)[g]

[a]LBPC-PPC, Université de Montpellier, INM INSERM, IRMB CHU de Montpellier, Montpellier, France
[b]Université de Montpellier, Memory Research and Resources Center, Department of Neurology, Inserm INM, F-34000, Montpellier, France
[c]Sant Pau Memory Unit, Hospital de la Santa Creu i Sant Pau - Biomedical Research Institute Sant Pau - Universitat Autònoma de Barcelona, Barcelone, Spain
[d]CHU de Montpellier, Hôpital Lapeyronie, Biochimie, Montpellier, France
[e]CH Perpignan, Gériatrie, Perpignan, France
[f]CHU de Nîmes, Neurology, Nîmes, France

Summary

Background Early detection of brain amyloidosis (Aβ+) is crucial for diagnosing Alzheimer' disease (AD) and optimizing patient management, especially in light of emerging treatments. While plasma biomarkers are promising, their combined diagnostic value through specific ratios remains underexplored. In this study, we assess the diagnostic accuracy of plasma pTau isoform (pTau181 and pTau217) to Aβ42 ratios in detecting Aβ+ status.

Methods This study included 423 participants from the multicenter prospective ALZAN cohort, recruited for cognitive complaints. Aβ+ status was determined using cerebrospinal fluid (CSF) biomarkers. The confirmatory cohort comprises 1176 patient samples from the Alzheimer's Disease Neuroimaging Initiative (ADNI), with Aβ+ status determined by positron emission tomography (PET) imaging. Plasma biomarkers (pTau181, pTau217, Aβ40, Aβ42) were measured using immunoassays and mass spectrometry, with specific ratios calculated. In the ALZAN cohort, the impact of confounding factors such as age, renal function, ApoE 4 status, body mass index, and the delay between blood collection and processing was also evaluated to assess their influence on biomarker concentrations and diagnostic performance. The primary outcome was the diagnostic performance of plasma biomarkers and their ratios for detecting Aβ+ status. Secondary outcomes in the ALZAN cohort included the proportion of patients classified as low, intermediate, or high risk for Aβ+ using a two-cutoff approach.

Findings In ALZAN the pTau181/Aβ42 ratio matched the diagnostic performance of pTau217 (AUC of 0.911 (0.882–0.940) vs. 0.909 (0.879–0.939), P = 0.85). The pTau217/Aβ42 ratio demonstrated the highest diagnostic accuracy, with an AUC of 0.927 (0.900–0.954). Both ratios effectively mitigated confounding factors, such as variations in renal function, and were also efficient in identifying Aβ+ status in individuals with early cognitive decline. Diagnostic accuracy of ratios vs. individual measurement was confirmed in the ADNI cohort. In ALZAN, using two-cutoff workflows with pTau217/Aβ42 instead of pTau217 alone reduced the intermediate-risk zone from ~16% to ~8%, enhancing stratification for clinical decision-making.

Interpretation The pTau217/Aβ42 ratio demonstrated improved diagnostic performance for detecting Aβ+ compared to individual biomarkers, potentially reducing diagnostic uncertainty. These findings suggest that plasma biomarker ratios could be useful; however, further validation in independent and diverse clinical settings is necessary before broader clinical implementation.

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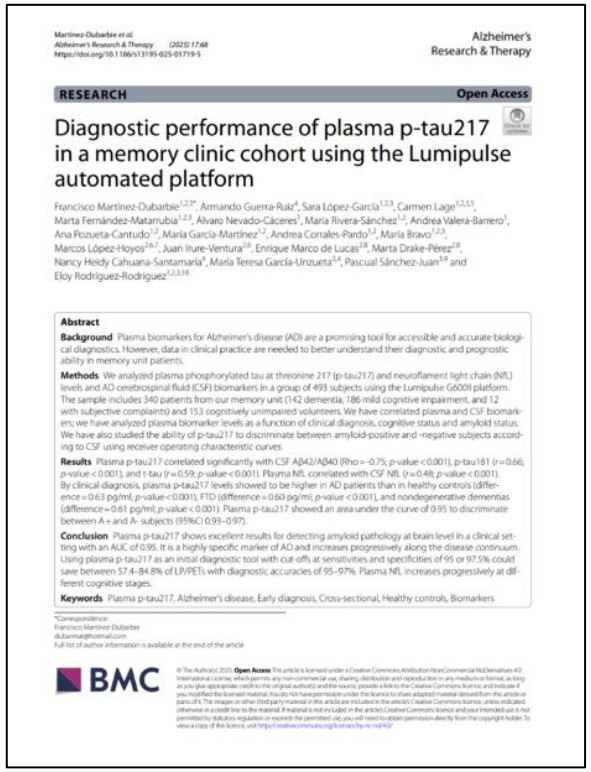
[g]Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Publication_Agreement_List.pdf.



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Alzheimer's Research & Therapy

RESEARCH Open Access

Diagnostic performance of plasma p-tau217 in a memory clinic cohort using the Lumipulse automated platform

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Abstract

Background Plasma biomarkers for Alzheimer's disease (AD) are a promising tool for accessible and accurate biological diagnostics. However, data in clinical practice are needed to better understand their diagnostic and prognostic ability in memory unit patients.

Methods We analyzed plasma phosphorylated tau at threonine 217 (p-tau217) and neurofilament light chain (NfL) levels and AD cerebrospinal fluid (CSF) biomarkers in a group of 493 subjects using the Lumipulse G600II platform. The sample includes 340 patients from our memory unit (142 dementia, 186 mild cognitive impairment, and 12 with subjective complaints) and 153 cognitively unimpaired volunteers. We have correlated plasma and CSF biomarkers; we have analyzed plasma biomarker levels as a function of clinical diagnosis, cognitive status and amyloid status. We have also studied the ability of p-tau217 to discriminate between amyloid-positive and -negative subjects according to CSF using receiver operating characteristic curves.

Results Plasma p-tau217 correlated significantly with CSF Aβ42/Aβ40 (Rho = -0.75; p-value < 0.001), p-tau181 (r = 0.66; p-value < 0.001), and t-tau (r = 0.59; p-value < 0.001). Plasma NfL correlated with CSF NfL (r = 0.48; p-value < 0.001). By clinical diagnosis, plasma p-tau217 levels showed to be higher in AD patients than in healthy controls (difference = 0.63 pg/mL p-value < 0.001), FTD (difference = 0.60 pg/mL p-value < 0.001), and nondegenerative dementias (difference = 0.61 pg/mL p-value < 0.001). Plasma p-tau217 showed an area under the curve of 0.95 to discriminate between A + and A- subjects (95%CI 0.93–0.97).

Conclusion Plasma p-tau217 shows excellent results for detecting amyloid pathology at brain level in a clinical setting with an AUC of 0.95. It is a highly specific marker of AD and increases progressively along the disease continuum. Using plasma p-tau217 as an initial diagnostic tool with cut-offs at sensitivities and specificities of 95 or 97.5% could save between 57.4–84.8% of LP/PETs with diagnostic accuracies of 95–97%. Plasma NfL increases progressively at different cognitive stages.

Keywords Plasma p-tau217, Alzheimer's disease, Early diagnosis, Cross-sectional, Healthy controls, Biomarkers

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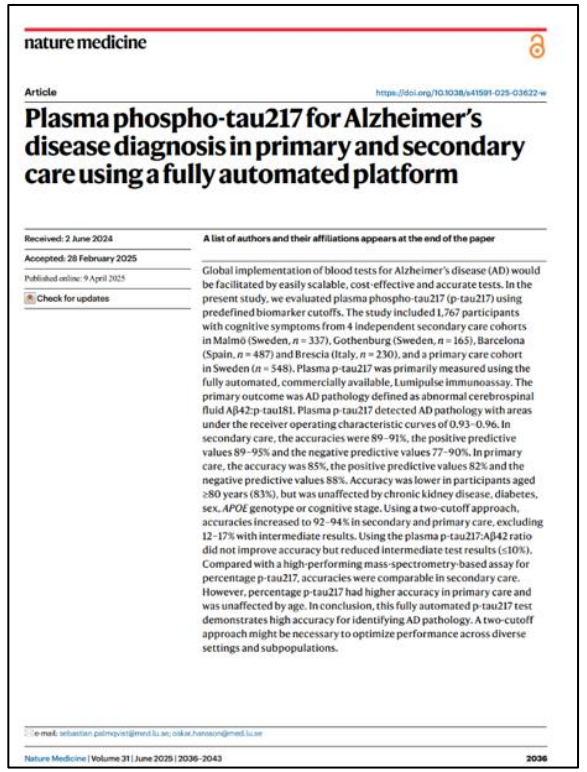

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Plasma phospho-tau217 for Alzheimer's disease diagnosis in primary and secondary care using a fully automated platform

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Global implementation of blood tests for Alzheimer's disease (AD) would be facilitated by easily scalable, cost-effective and accurate tests. In the present study, we evaluated plasma phospho-tau217 (p-tau217) using predefined biomarker cutoffs. The study included 1,767 participants with cognitive symptoms from 4 independent secondary care cohorts in Malmö (Sweden, n = 337), Gothenburg (Sweden, n = 165), Barcelona (Spain, n = 487) and Brescia (Italy, n = 230), and a primary care cohort in Sweden (n = 548). Plasma p-tau217 was primarily measured using the fully automated, commercially available, Lumipulse immunoassay. The primary outcome was AD pathology defined as abnormal cerebrospinal fluid Aβ42:p-tau181. Plasma p-tau217 detected AD pathology with areas under the receiver operating characteristic curves of 0.93–0.96. In secondary care, the accuracies were 89–91%, the positive predictive values 89–95% and the negative predictive values 77–90%. In primary care, the accuracy was 85%, the positive predictive values 82% and the negative predictive values 88%. Accuracy was lower in participants aged ≥80 years (83%), but was unaffected by chronic kidney disease, diabetes, sex, *APOE* genotype or cognitive stage. Using a two-cutoff approach, accuracies increased to 92–94% in secondary and primary care, excluding 12–17% with intermediate results. Using the plasma p-tau217:Aβ42 ratio did not improve accuracy but reduced intermediate test results (≤10%). Compared with a high-performing mass-spectrometry-based assay for percentage p-tau217, accuracies were comparable in secondary care. However, percentage p-tau217 had higher accuracy in primary care and was unaffected by age. In conclusion, this fully automated p-tau217 test demonstrates high accuracy for identifying AD pathology. A two-cutoff approach might be necessary to optimize performance across diverse settings and subpopulations.

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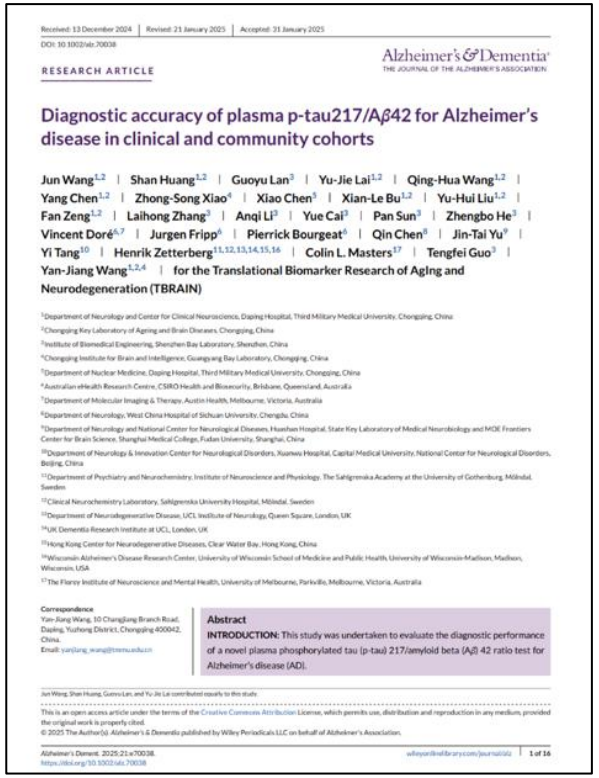

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RESEARCH ARTICLE

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Diagnostic accuracy of plasma p-tau217/Aβ42 for Alzheimer's disease in clinical and community cohorts

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Abstract

INTRODUCTION: This study was undertaken to evaluate the diagnostic performance of a novel plasma phosphorylated tau (p-tau) 217/amyloid beta (Aβ) 42 ratio test for Alzheimer's disease (AD).

Jun Wang, Shan Huang, Guoyu Lan, and Yu-Jie Lai contributed equally to this study.

Case study in Alzheimer's Disease

Patient: 72-year-old woman who personally doesn't recognize any problem

Family suggests a 1-3 year history of memory impairment:

- Problems word-finding
- Cannot cook a meal she's prepared 1000 times, rechecks recipe repeatedly
- Forgets what she did the day before
- Needs to be told more than once about appointments
- Decline in "keeping house" according to family
- Less interested/ motivated to go out.

PMHx: HTN / HLD / "pre-diabetic"
Exam: Normal / non-focal
MMSE 25/30 forgot all 3 words in recall, spelled WORLD backwards as "D L O R W"
PHQ-9 = 4 (Feeling tired/having little energy)
Meds: losartan, rosuvastatin, NKDA
Family hx: Mom and paternal grandfather "had dementia".
Social hx: Married. Lives with husband. Two kids live nearby.
Work: Retired at age 65 with no concerns by employer at that time.
Education: High School diploma, no specific education since
Tobacco: None
Alcohol: "glass of wine at night with dinner"

Tests ordered

Labs:
- CBC, Chem panel and TSH all normal
- B12 borderline, but still normal
- Fasting blood sugar 112

MRI Brain:
- Mild white matter changes
- Mild generalized atrophy
- Volumetrics: Hippocampal volume 3rd percentile for age
- Ventricles consistent with the degree of atrophy

Neuropsych testing:
- Mild Cognitive Impairment, NOS
- Mild depression

BBM testing to aid in detection of amyloid pathology

How does the test result change what you would do next…?

Scenario 1

- Negative test result using a BBM test that has a high false negative rate

BBM testing to aid in detection of amyloid pathology

How does the test result change what you would do next…?

Scenario 1

- Negative test result using a BBM test that has a high false negative rate

Scenario 2

- Indeterminate BBM test result

BBM testing to aid in detection of amyloid pathology

How does the test result change what you would do next…?

Scenario 1

- Negative test result using a BBM test that has a high false negative rate

Scenario 2

- Indeterminate BBM test result

Scenario 3

- Positive test result using a BBM test that has a high false positive rate

BBM testing to aid in detection of amyloid pathology

How does the test result change what you would do next…?

Scenario 1

- Negative test result using a BBM test that has a high false negative rate

Scenario 2

- Indeterminate BBM test result

Scenario 3

- Positive test result using a BBM test that has a high false positive rate

Scenario 4

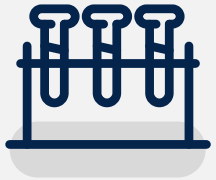
- Positive test result using a BBM test meeting 90% Sensitivity, 90% Specificity

Clinical limitations of biomarkers

Although biomarkers can diagnose AD in an asymptomatic individual, not all people who are amyloid positive qualify for treatment because a significant number:

- are “false positives” — even with the best of tests — they simply don’t have plaques/tangles
- have no symptoms — MCI and dementia are clinical diagnoses, not laboratory diagnoses
- have a mixed dementia — reasons other than the plaques/tangles to explain their dementia — and therefore removing plaque is not enough
- some are simply too demented to see benefit and/or the risk(s) of therapy are too high to be appropriate

Advances in blood biomarkers are driving the Alzheimer's disease landscape forward and clinical use cases will continue to evolve



BBMs are increasingly accurate for documenting amyloid pathology and may improve early diagnosis rates

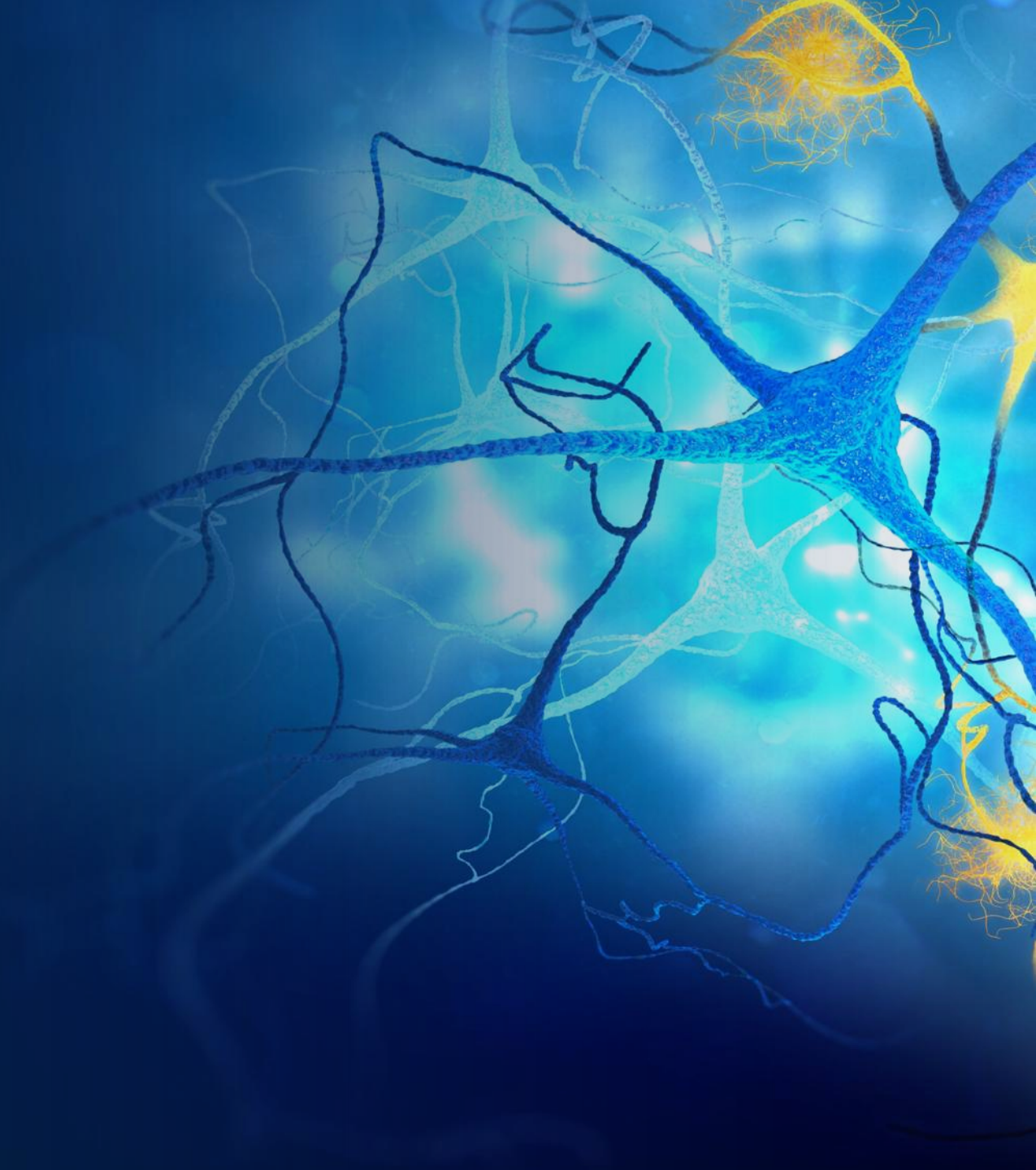
Validated BBM tests are likely to improve access to emerging treatment options

BBMs used during screening for clinical trials may accelerate enrollment and reduce costs

BBMs are being explored for other purposes as well, e.g., monitoring treatment response and determining prognosis for at-risk individuals

BBM, blood biomarker.
Hampel H et al. Neuron. 2023;111(18):2781–2799.

Thank you!



Questions

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Recording

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WEBINAR 1: Demystifying Alzheimer's Blood Biomarkers: What Every Clinician Needs to Know

Live Event: Tuesday, December 9, 2025 | 1:00 pm – 2:00 pm EST

P.A.C.E.® Credit available until June 9, 2026 | Florida Lab Credit available

Recording

Slides

This foundational webinar will clarify the science and clinical role of blood-based biomarkers (BBMs) in Alzheimer's disease (AD). Analytical and clinical performance of AD BBM tests and appropriate positioning of testing within recommended diagnostic pathways alongside cognitive assessment, rule-out labs, and other testing modalities (PET/CSF) will be discussed. Special emphasis will be placed on interpreting positive, indeterminate, and negative test results. Included is a case-based dialogue to address common myths, patient communication tips, and how BBMs enable earlier access to specialist care and potential disease-modifying therapies.

Objectives:

- Differentiate AD BBM tests and key performance characteristics for amyloid pathology detection.
- Identify appropriate clinical use scenarios to order AD BBM tests within a structured diagnostic workup.
- Compare AD BBM tests to PET and CSF for amyloid/tau confirmation.
- Interpret positive, negative and indeterminate test results to guide patient management and patient/caregiver consultations.

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Demystifying Alzheimer's Blood Biomarkers

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