MAYO CLINIC
LABORATORIES

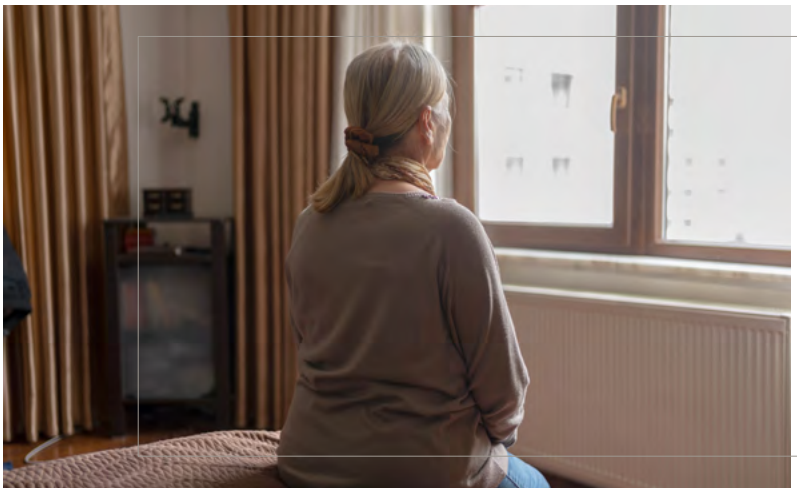
# Dementia fluid biomarker testing

A complete dementia workup from one trusted lab

# Contents

# A growing concern

## The physical, mental, and emotional toll of Alzheimer's disease is tremendous.



**60–80%**

of dementia patients have Alzheimer's disease[1]

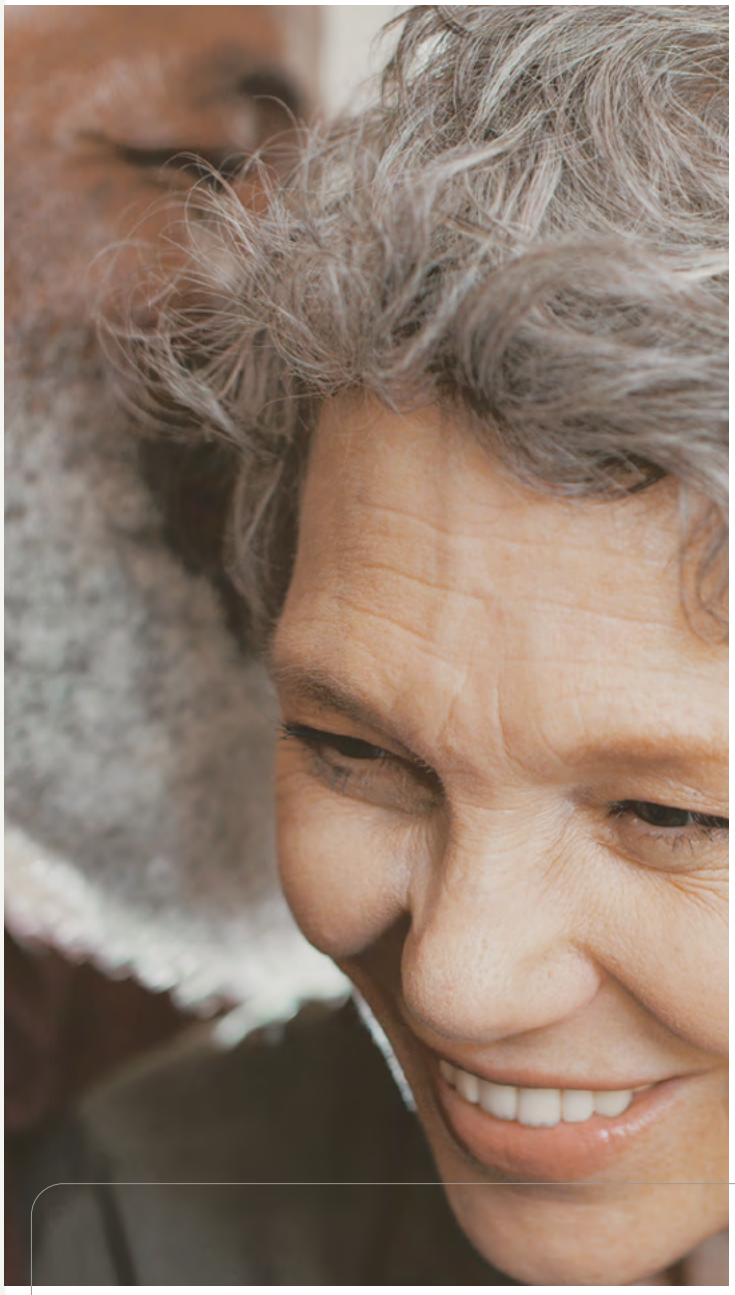
**1 in 3**

seniors worldwide dies with dementia[1]

**$2.8T**

estimated global financial burden of Alzheimer's disease and related dementias[2]

# And the impact of Alzheimer's is only expanding



By 2055, the total number of people with Alzheimer's disease is expected to increase by

**150%**[1]

By 2050, healthcare costs associated with Alzheimer's care globally are estimated to reach more than

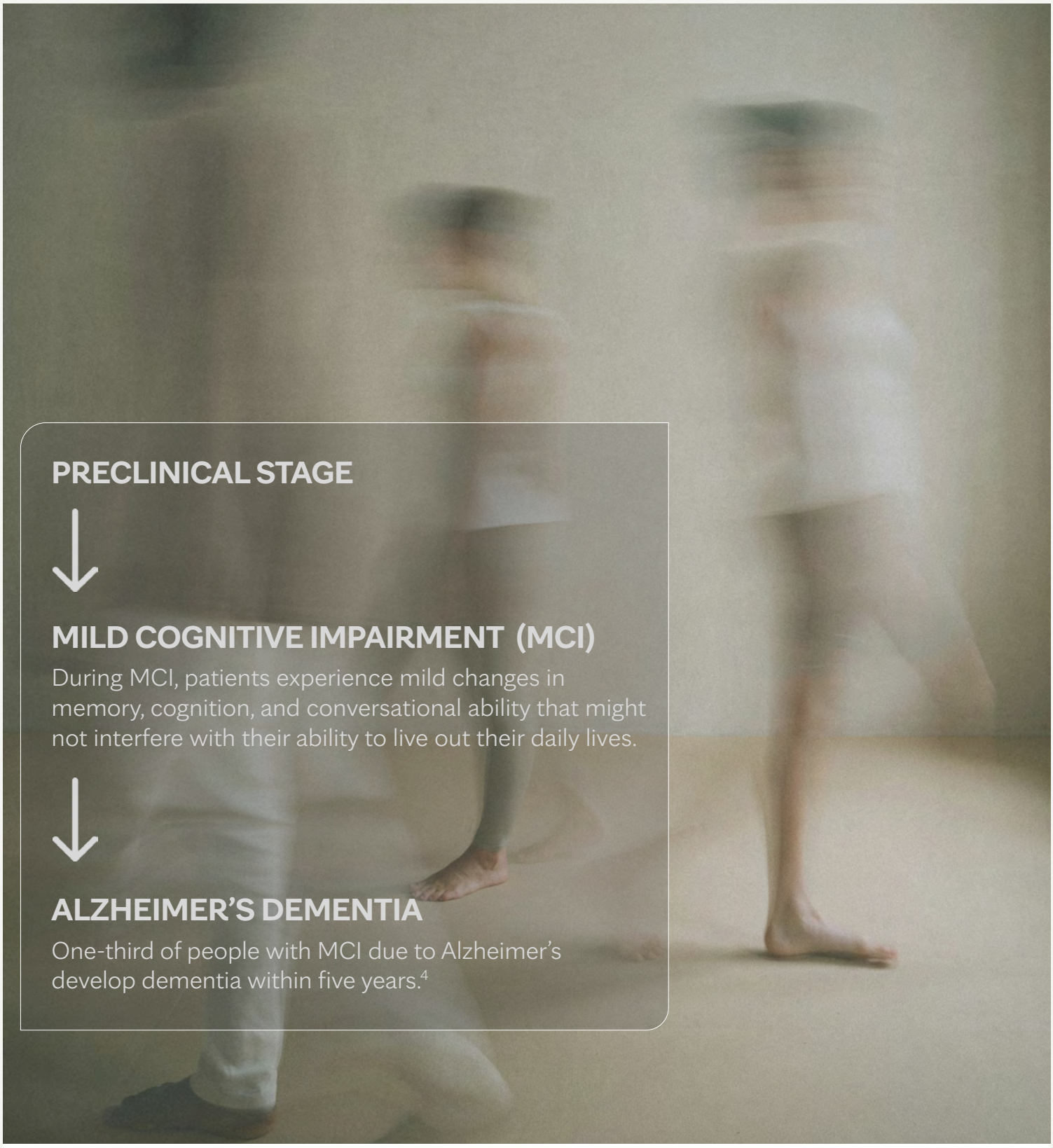
**$16.6T**[3]

Alzheimer's disease affects each individual differently.

Average age of diagnosis is 65.

On average people live for eight years after diagnosis.

Some individuals live 20 years or more.



## PRECLINICAL STAGE

## MILD COGNITIVE IMPAIRMENT (MCI)

During MCI, patients experience mild changes in memory, cognition, and conversational ability that might not interfere with their ability to live out their daily lives.

## ALZHEIMER'S DEMENTIA

One-third of people with MCI due to Alzheimer's develop dementia within five years.[4]

# **A uniformly devastating disease**

Everyone with Alzheimer's goes through several disease stages.

## **Time is of the essence.**

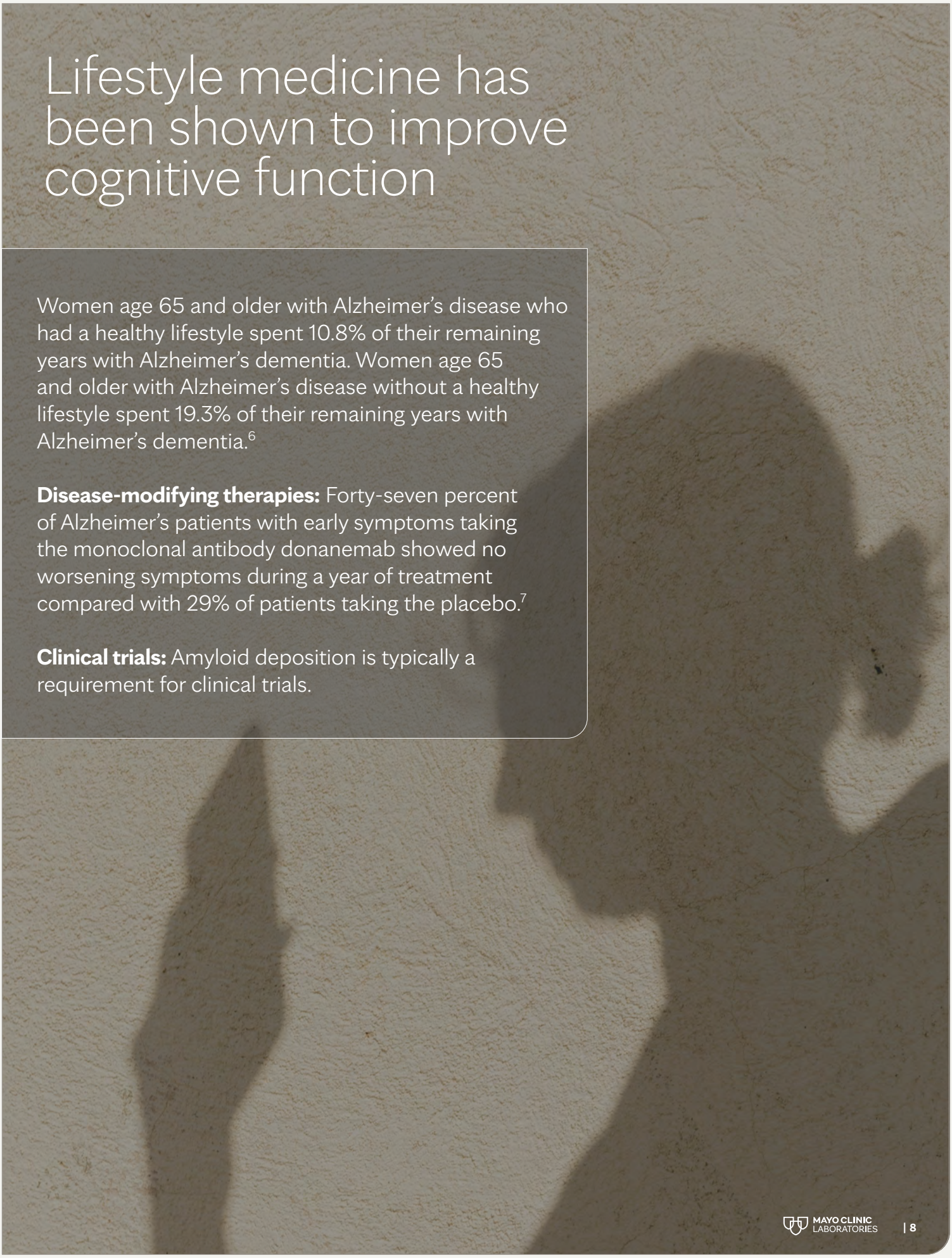
Identifying Alzheimer's disease at the onset of MCI, before dementia sets in, can provide hope and a plan for the future. Early diagnosis through laboratory testing can give patients more time with loved ones and to prepare for what's ahead.

# Lifestyle medicine has been shown to improve cognitive function

Women age 65 and older with Alzheimer's disease who had a healthy lifestyle spent 10.8% of their remaining years with Alzheimer's dementia. Women age 65 and older with Alzheimer's disease without a healthy lifestyle spent 19.3% of their remaining years with Alzheimer's dementia.[6]

**Disease-modifying therapies:** Forty-seven percent of Alzheimer's patients with early symptoms taking the monoclonal antibody donanemab showed no worsening symptoms during a year of treatment compared with 29% of patients taking the placebo.[7]

**Clinical trials:** Amyloid deposition is typically a requirement for clinical trials.



# Empowering providers

Testing for cerebrospinal fluid biomarkers to identify brain amyloid pathology has been the standard for detection. These tests can have drawbacks: cost, patient health risks due to the invasive nature of specimen collection, and lack of access to a facility and/or clinician to perform the specimen collection.

Laboratory tests for Alzheimer's disease fluid biomarkers that have high concordance to amyloid PET allow physicians to more accurately diagnose MCI and dementia due to Alzheimer's disease.

## Testing to improve diagnostic accuracy

Conventional diagnostic tools

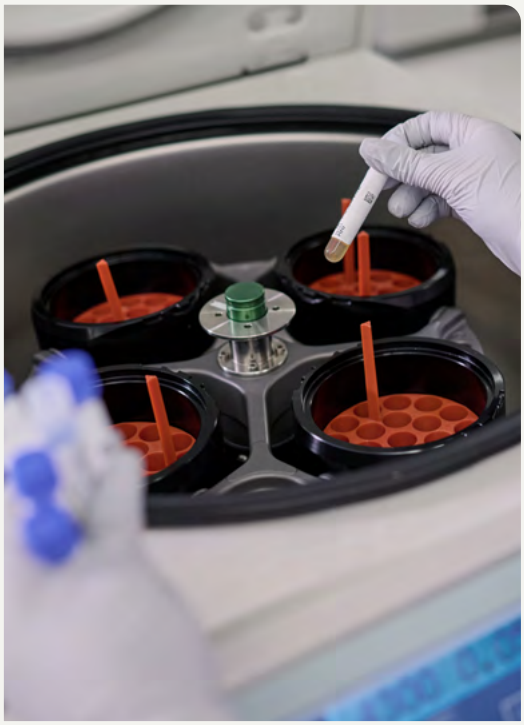
61%

**Only 61%** of Alzheimer's disease cases were accurately diagnosed by primary care physicians[1]

Addition of AD fluid-biomarker testing

>90%

**More than 90%** of Alzheimer's disease cases were accurately diagnosed[9,10]



# A proactive approach

The discovery that phosphorylated Tau proteins in the blood can identify brain amyloid pathology propelled the development of plasma-based biomarker testing. Accurate answers enable earlier intervention.

- Fast time to results
- Cost savings
- Noninvasive
- Improved accuracy

# Innovating at the edge of discovery

Mayo Clinic Laboratories' plasma biomarker testing uses the clinically supported p-Tau217 protein to identify Aβ pathology. Research has revealed that p-Tau217 exhibits high diagnostic accuracy in predicting Aβ positivity.

Our p-Tau217 plasma biomarker assay is recommended for individuals over the age of 50 with mild cognitive impairment or early dementia.

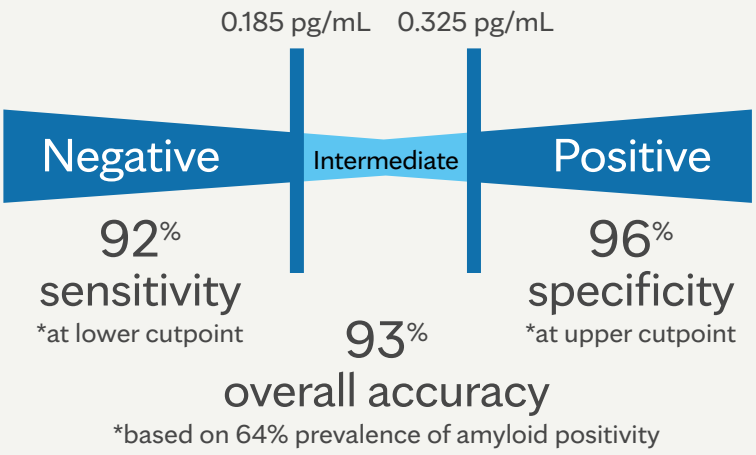
Clinical laboratory technician Meaghan Kroska examines tubes of patient plasma samples before processing.

# The highest level of diagnostic accuracy

Our p-Tau217 plasma biomarker test uses a two-cutpoint model that provides the highest standard for result interpretation.

Using two cutpoints enables increased sensitivity and specificity and overall greater accuracy than single cutpoint testing. Single model cutpoint testing performed in our laboratory failed to deliver 90% overall accuracy.[11]

**Two-cutpoint result interpretation**




Susan Ashrafzadeh Kian, clinical laboratory technician, prepares serum samples for plasma biomarker testing in the Clinical Immunoassay Laboratory at Mayo Clinic.

# Pioneering testing, precision results

In addition to Mayo Clinic Laboratories' plasma and cerebrospinal fluid (CSF) biomarker testing, we offer plasma biomarker testing from C2N Diagnostics and CSF biomarker testing from Amprion.

- Ratio of Aβ42/Aβ40
- Ratio of p-Tau217/np-Tau217 (%p-Tau217) in plasma
- *APOE* genotype in plasma
- Alpha-synuclein protein aggregates in CSF

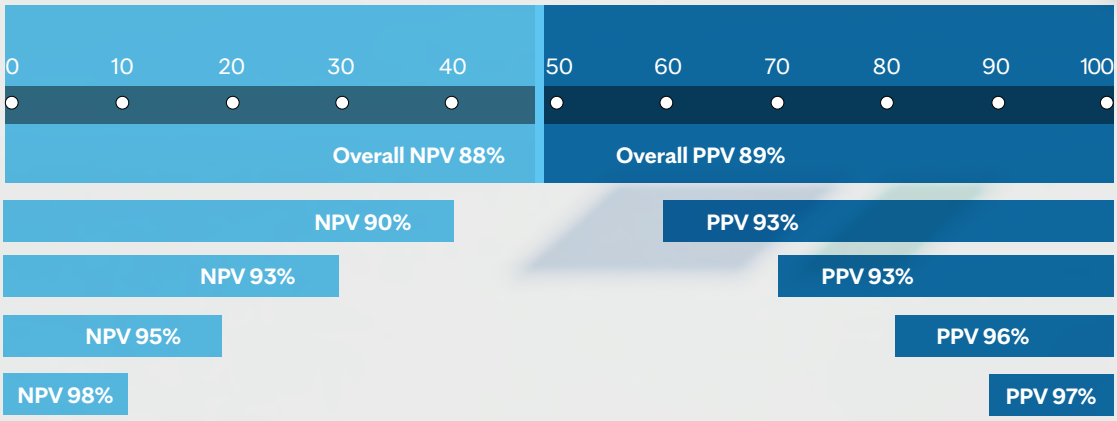

# PrecivityAD2™

- Uses highly accurate liquid chromatography-tandem mass spectrometry to measure Aβ42, Aβ40, p-Tau217, and np-Tau217.
- Combines two ratios — Aβ42/40 and %p-Tau217 (p-Tau217/np-Tau217) — into a clinically and analytically validated algorithm to generate the amyloid probability score 2 (APS2).
- Single APS2 cutpoint optimized to obtain an overall 88% sensitivity and 89% specificity. At an observed disease prevalence of 53%, the test achieves 88% overall accuracy, 90% PPV, and 87% NPV.

# Precivity AD2™, Reflex to Apolipoprotein

- Identical to Precivity AD2™, but reflexes to apolipoprotein E (ApoE) proteotyping to determine *APOE E4* status.

## Amyloid Probability Score 2 Performance*

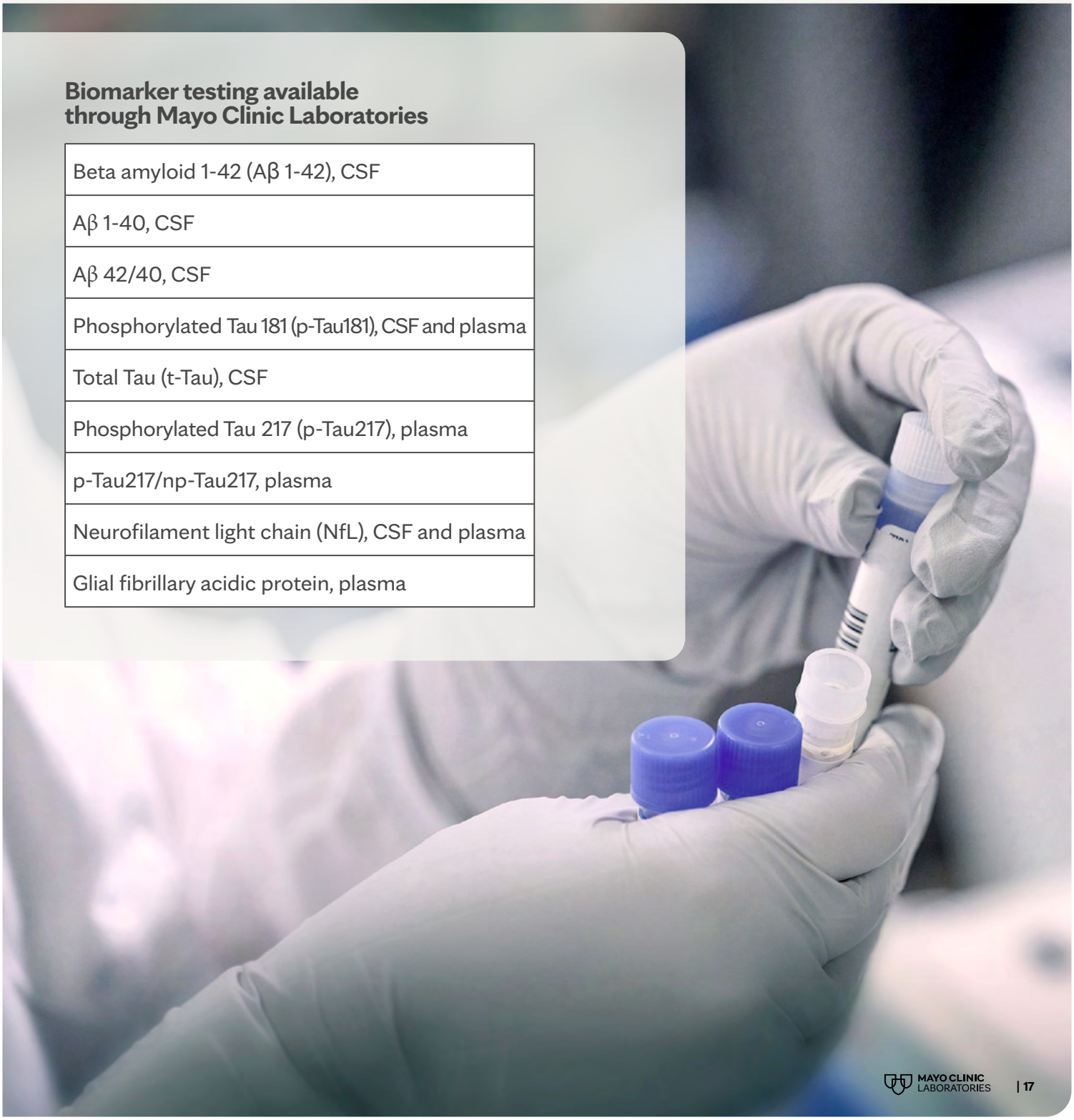



*Based on 50% prevalence of amyloid positivity

# SAAmplify™-αSYN

- Uses an innovative seed-amplification assay to detect misfolded alpha-synuclein aggregates in cerebrospinal fluid with autopsy-confirmed accuracy.
- Offers 96% sensitivity and 92% specificity in the detection of α-synuclein pathology.[11]
- Provides differential clarity to rule out many Parkinson's disease mimics and Alzheimer's disease with Lewy body mixed pathology (AD-LB).
    - Detected-1 result indicates neuronal synuclein disease (e.g., Parkinson's disease, AD-LB, and dementia with Lewy bodies [DLB]).
    - Detected-2 result is consistent with pathology found mainly in patients with multiple system atrophy.
    - A not detected result indicates misfolded alpha-synuclein was not detected.

# Comprehensive dementia testing solution



## Biomarker testing available through Mayo Clinic Laboratories

| |
|---|
| Beta amyloid 1-42 (Aβ 1-42), CSF |
| Aβ 1-40, CSF |
| Aβ 42/40, CSF |
| Phosphorylated Tau 181 (p-Tau181), CSF and plasma |
| Total Tau (t-Tau), CSF |
| Phosphorylated Tau 217 (p-Tau217), plasma |
| p-Tau217/np-Tau217, plasma |
| Neurofilament light chain (NfL), CSF and plasma |
| Glial fibrillary acidic protein, plasma |

# Examine other causes

For patients with symptoms of early-onset Alzheimer's disease or those with a strong family history of the condition, genetic testing may be beneficial.[12,13]

- Early-onset familial genes, such as *APP, PSEN1,* and *PSEN2*, may be considered. These genes are deterministic for 1% of Alzheimer's disease cases.
- 10%–15% of early-onset dementia cases are associated with changes in *APP, PSEN1,* and *PSEN2*.
- The *APOE4* variant has a dose-dependent effect on the risk of side effects for patients on anti-amyloid treatments. Assessment of the *APOE* genotype is recommended for individuals being considered for anti-amyloid monoclonal antibody treatments.

Co-directors of the Clinical Immunoassay Laboratory at Mayo Clinic Laboratories, Joshua Bornhorst, Ph.D., and Alicia Algeciras-Schimnich, Ph.D., review results from plasma biomarker testing.

In cases where Alzheimer's biomarker or genetic testing does not provide definitive answers, Mayo Clinic Laboratories offers a **full portfolio of dementia assays**.

| | | | | | |
|---|---|---|---|---|---|
| **Alzheimer's disease** | p-Tau217 plasma biomarker testing | C2N plasma biomarker testing | Cerebrospinal fluid biomarker testing | | |
| **Synucleinopathies** | Alpha-synuclein aggregates in CSF | | | | |
| **Prion disease** | Rapidly progressive dementia | Creutzfeldt-Jakob disease | | | |
| **Autoimmune dementia** | Autoimmune and paraneoplastic antibody testing | | | | |
| **Genetic testing** | Apolipoprotein E genotyping | *Notch3* full gene analysis | *SOD1* gene for frontotemporal dementia and amyotrophic lateral sclerosis | *C9orf72* hexanucle-otide | *APP, PSEN1, PSEN2* |
| **Neurodegeneration marker** | Neurofilament light chain | Glial fibrillary acidic protein | | | |

# Unmatched expertise and experience

The collaboration of Mayo Clinic Laboratories with the Mayo Clinic behavioral neurology practice enables the development of the most clinically relevant tests. Our dementia physicians, laboratory scientists, and genetic counselors are available to consult or answer questions on complex cases.

**Access the industry's most sophisticated dementia test menu.**

Alicia Algeciras-Schimnich, Ph.D., professor of laboratory medicine and pathology and co-director of the Clinical Immunoassay Laboratory at Mayo Clinic Laboratories

# References


[1]2024 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2024 May;20(5):3708-3821. doi:10.1002/alz.13809. Epub 2024 Apr 30. PMID: 38689398; PMCID: PMC11095490. [2]Wong W. Economic burden of Alzheimer's disease and managed care considerations. *Am J Manag Care.* 2020;26:S177-S183. https://doi.org/10.37765/ajmc.2020.88482 [3]Nandi A, Counts N, Chen S, et al. Global and regional projections of the economic burden of Alzheimer's disease and related dementias from 2019 to 2050: A value of statistical life approach. *Lancet.* Sept 2022;51:101580. https://doi.org/10.1016/j.eclinm.2022.101580 [4]Liu Y, Jun H, Becker A, et al. Detection rates of mild cognitive impairment in primary care for the United States Medicare population. *J Prev Alzheimers Dis.* 2024;11(1):7–12. https://doi.org/10.14283/jpad.2023.131 [5]Ornish D, Madison C, Kivipelto M, et al. Effects of intensive lifestyle changes on the progression of mild cognitive impairment or early dementia due to Alzheimer's disease: a randomized, controlled clinical trial. *Alz Res Therapy.* 2024 Jun 7;16(1):122. https://doi.org/10.1186/s13195-024-01482-z [6]Dhana K, Franco OH, Ritz EM, et al. Healthy lifestyle and life expectancy with and without Alzheimer's dementia: population based cohort study. *BMJ* 2022; 377:e068390 doi:10.1136/bmj-2021-068390 [7]Sims JR, Zimmer JA, Evans CD, et al. Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial. *JAMA.* 2023;330(6):512–527. doi:10.1001/jama.2023.13239 [8]Alzheimer's disease facts and figures. Alzheimer's Association. 2022 Alzheimer's Disease Facts and Figures. https://www.alz.org/alzheimers-dementia/facts-figures [9]Palmqvist S, Tideman P, Mattsson-Carlgren N, et al. Blood biomarkers to detect Alzheimer disease in primary care and secondary care. *JAMA*. 2024;332(15):1245–1257. doi:10.1001/jama.2024.13855 [10]Ashton NJ, Brum WS, Di Molfetta G, et al. Diagnostic accuracy of a plasma phosphorylated tau 217 immunoassay for Alzheimer disease pathology. *JAMA Neurol.* 2024 Mar 1;81(3):255-263. doi:10.1001/jamaneurol.2023.5319. PMID: 38252443; PMCID: PMC10804282. [11]Ma Y, Farris C, Weber S, et al. Sensitivity and specificity of a seed amplification assay for diagnosis of multiple system atrophy: a multicentre cohort study. *Lancet Neurol*. 2024 Dec;23(12):1225-1237. [12]Rossi M, Candelise N, Baiardi S, et al. Ultrasensitive RT-QuIC assay with high sensitivity and specificity for Lewy body-associated synucleinopathies. *Acta Neuropathol.* 2020 Jul;140(1):49-62. https://doi.org/10.1007/s00401-020-02160-8. Epub 2020 Apr 27. Erratum in: *Acta Neuropathol.* 2020 Aug;140(2):245. https://doi.org/10.1007/s00401-020-02170-6 PMID: 32342188; PMCID: PMC7299922. [13]Vaughan, D, Fumi, R, Theilmann Jensen, M, et al. Evaluation of cerebrospinal fluid α-synuclein seed amplification assay in progressive supranuclear palsy and corticobasal syndrome. *Mov Disord.* 2024 39: 2285-2291. https://doi.org/10.1002/mds.30019 [14]Andrade-Guerrero J, Santiago-Balmaseda A, Jeronimo-Aguilar P, et al. Alzheimer's disease: an updated overview of its genetics. *Int J Mol Sci.* 2023 Feb 13;24(4):3754. doi:10.3390/ijms24043754. PMID: 36835161; PMCID: PMC9966419. [15]Alzheimer's Disease Genetics Fact Sheet. National Institute on Aging. https://www.nia.nih.gov/health/genetics-and-family-history/alzheimers-disease-genetics-fact-sheet. Reviewed March 2023. Accessed June 2024.

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