OMG...I DIDN'T KNOW THAT!

Alzheimer's disease:
Simple blood test, diagnostic clarity

PODCAST 49 & 50

Early & simple detection and diagnosis of Alzheimer's disease is important to many patients

99%

Nearly all Americans said it is important to diagnose Alzheimer's disease (AD) in the **early stages**.

83%

83% of Americans would undergo simple medical testing for AD because it would allow for **earlier treatment and care**, and knowing would:

76% allow for planning

68% encourage action to preserve existing cognitive function

67% help understand what is happening.

9/10

Most Americans want a **simple** medical test, e.g., a blood-based biomarker test to detect AD if it were available.

79%

79% of Americans want to know if they have AD **before** experiencing symptoms or symptoms interfere with daily activities.

80%

80% of Americans said **they would ask** for a simple medical test **rather than wait** for their doctor to suggest it.

Alzheimer's Association. 2025 Alzheimer's Disease Facts and Figures. *Alzheimers Dement* 2025;21(5).

Blood-based biomarkers in Alzheimer’s disease

Biomarker	Methods and process	Remarks
Beta amyloid 1–42/beta amyloid 1–40 (Aβ42/Aβ40) ratio	Mass spectrometry assays, immunoassays	A decline in Aβ42 levels is indicative of amyloid accumulation in the brain
	Cerebral Aβ pathology	A lower Aβ42/Aβ40 ratio aligns closely with amyloid deposition as identified by amyloid PET imaging
		There is a high correlation between cerebrospinal fluid (CSF) and blood Aβ42/Aβ40 levels
Phosphorylated tau protein (P-tau)	Mass spectrometry assays, immunoassays	P-tau levels are increased in both manifest and asymptomatic stages of Alzheimer’s disease
	Neuronal tau phosphorylation and secretion	There is a significant correlation between CSF and blood levels of P-tau
Subtypes of P-tau (P-tau 181, P-tau-217, P-tau-205, P-tau231)	Mass spectrometry assays, immunoassays neuronal tau phosphorylation and secretion	Variants of phosphorylated tau protein, including P-tau 181, P-tau 217, P-tau 205, and P-tau 231, show increased levels in both symptomatic and asymptomatic Alzheimer’s disease.
		These subtypes of P-tau are highly sensitive and specific markers for Alzheimer’s disease
Neurofilament light (NfL) protein	Immunoassays, neurodegeneration	NfL mirrors the pathology of neurofibrillary tangles and the overall severity of Alzheimer’s disease
		There is a close correlation between CSF concentrations of NfL and its levels in Alzheimer’s disease
Glial fibrillary acidic protein (GFAP)	Immunoassays, astrocyte activation	GFAP indicates the presence of neuroinflammation and neurodegeneration
		The levels of GFAP in the plasma are indicative of the extent of astrogliosis

Arslan B, et al. *Clin Chem Lab Med.* 2024 Jan 23;62(6):1063-1069.

Mr. C: Presentation

- Presented to a neurologist at 72.
- He expressed no concerns, but his wife noticed difficulties with verbal communications:
  - Finding words during speech
  - Using the wrong words
  - Difficulty remembering names
- Both Mr. C and his wife suggest the difficulty has progressed over the past several years.

Mr. C: History

- History of high blood pressure
- No recent use of alcohol, tobacco, or other drugs
- Mr. C's mother died at 67 of supposed vascular dementia, but possibly due to AD
- Mr. C's father died at 79 of a heart attack
- Two older siblings have no known mental or cognitive abnormalities

Honig LS, Chin SS. *Sci Aging Environ*. 2001;dn2.

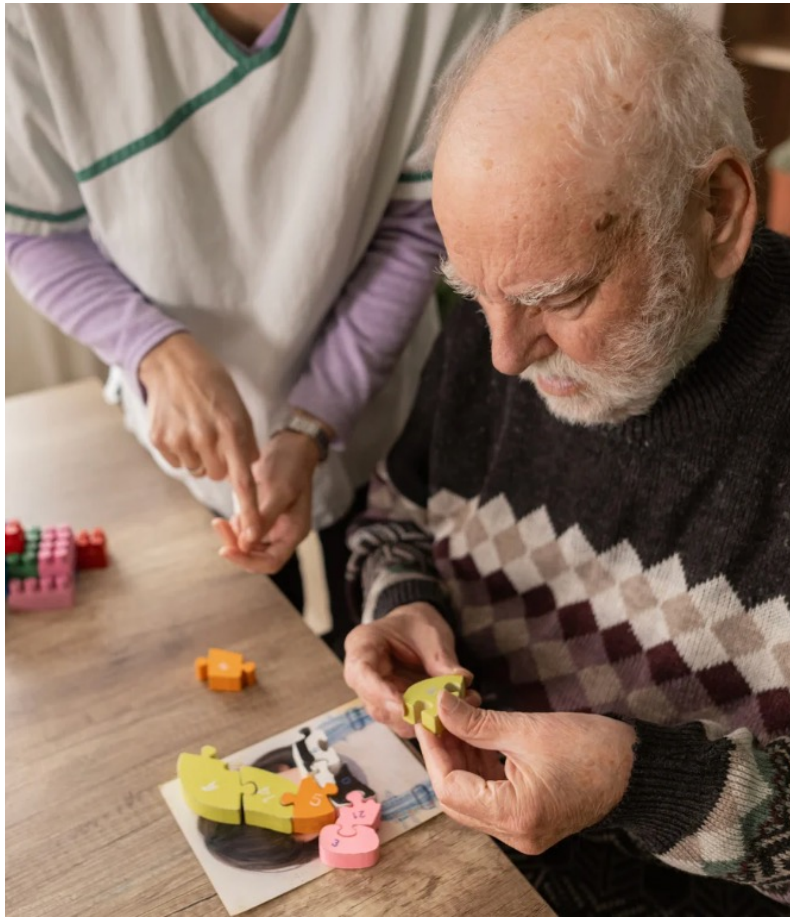
Mr. C: Mild changes in cognitive and social functioning

- Mr. C still worked as a business professional but experienced mild difficulties understanding what was being said to him and with his writing abilities.
- He handled household finances and long-standing chores without difficulty but needed additional instruction for new tasks.
- Self-care was normal and did not require prompting.
- Only when questioned, did he express concern about memory—specifically short-term memory.
- He had increased repetitious behavior and difficulty driving to new locations.
- He was slightly more irritable and had less interest in new activities, but his personality was otherwise normal and unchanged.

Honig LS, Chin SS. *Sci Aging Environ*. 2001;dn2.

Mr. C: Office neurological examination

- Mild difficulties in concentration and language usage
  - Incorrect words in spontaneous speech
  - Difficulty naming pictured objects, but could describe the object
  - Utilization of sound to describe objects
  - Difficulty repeating complex sentences or spelling words backwards
- Some disorientation to location, but not to date and time
- Impaired arithmetic abilities
- Memory testing showed significant impairments
  - Unable to remember objects or names shown earlier or that were general knowledge
- No other neurological impairments were noted



Honig LS, Chin SS. *Sci Aging Environ*. 2001;dn2.

Mr. C: Laboratory and other testing

- Blood tests
  - **CBC, kidney and liver function, B12, TSH, TP –** normal range
  - **pTau-217/β-Amyloid ratio test –** positive
- Imaging
  - **Brain MRI** – normal structure and size for the patient's age
  - **Chest X-rays** – normal
- Neuropsychological testing
  - **Confirmed impairments:** memory for words/images, naming objects, repeating words, expressive speech, reading/writing/arithmetic
  - **No impairments:** abstract reasoning, visuospatial abilities, drawing

Honig LS, Chin SS. *Sci Aging Environ*. 2001;dn2.

Mr. C: Clinical diagnosis of AD

- Memory impairment
- Prominent language problems
- Positive plasma AD biomarkers
- No other evidence of alternate causes or co-morbid conditions to explain symptoms

Honig LS, Chin SS. *Sci Aging Environ*. 2001;dn2.

Mr. C: AD symptom course

At diagnosis

- Columbia-modified mini-mental status exam - 37 (normal - 57)
- Word-generating task - 10th percentile (normal > 50th percentile)

2 years after

- Conversation became frustrating and difficult
- Columbia-modified mini-mental status exam - 23 (normal - 57)
- Word-generating task - 1st percentile (normal > 50th percentile)

3 years after

- More confused
- Posture change – stooping, stiffness, unexplained falls
- Incontinence

4 years after

- Agitation with hospitalization and antipsychotic medications for outbursts
- No longer able to follow instructions
- Disoriented to place and time

5 years after

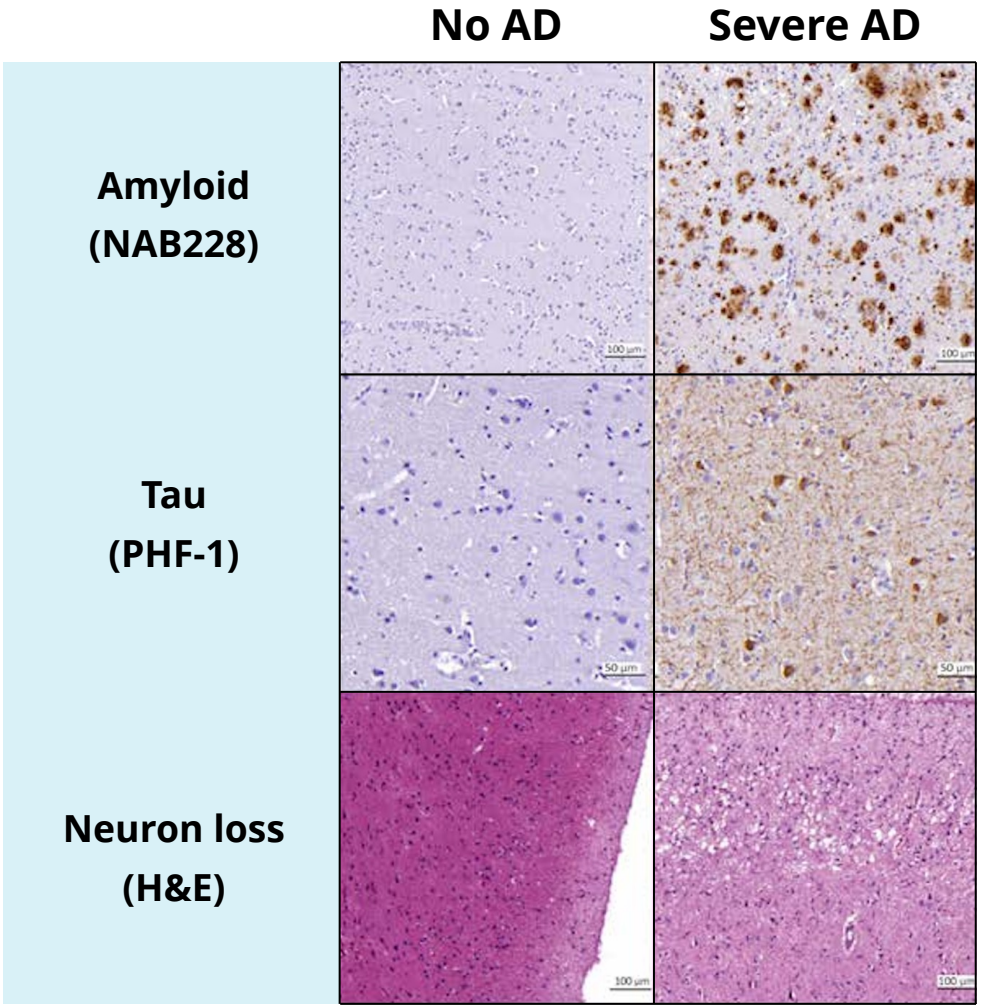
- Unwitnessed fall and hip fracture requiring surgical intervention
- Mr. C never walked again, developed infection
- Died one month later
- Autopsy showed a definitive diagnosis of AD

Honig LS, Chin SS. Sci Aging Environ. 2001;dn2.

Mr. C: AD confirmation

Autopsy showed a definitive diagnosis of AD

- Overall atrophy
- Enlarged ventricles
- β-amyloid and neuritic plaques
- Neurofibrillary tangles
- Pyramidal cell degeneration
- Temporal lobe neuropil threads of tau
- Amyloid angiopathy

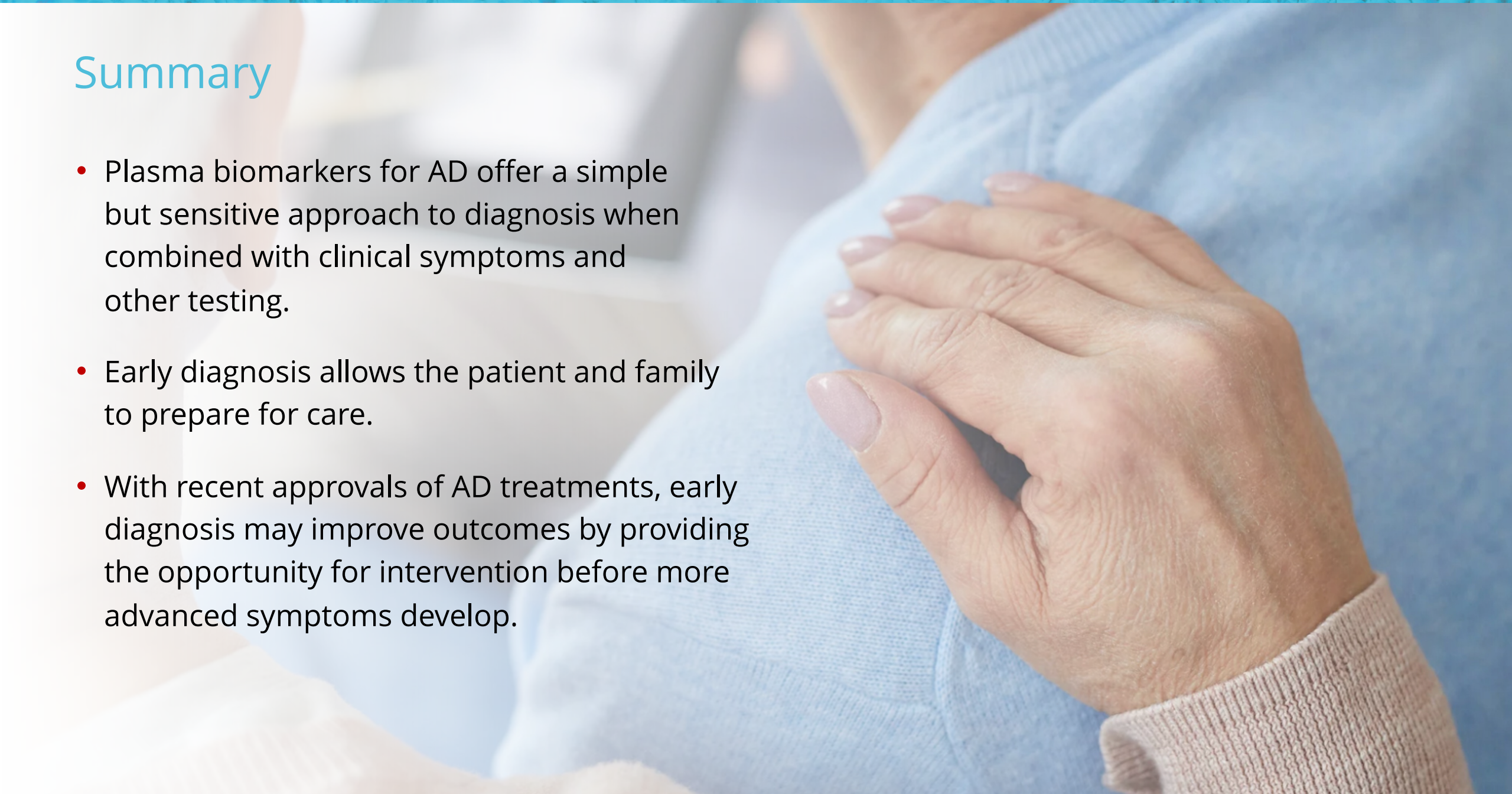


Honig LS, Chin SS. *Sci Aging Environ*. 2001;dn2.

Khandelwal P, et al. *Imag Neurosci*. 2024;2.

Summary

- Plasma biomarkers for AD offer a simple but sensitive approach to diagnosis when combined with clinical symptoms and other testing.
- Early diagnosis allows the patient and family to prepare for care.
- With recent approvals of AD treatments, early diagnosis may improve outcomes by providing the opportunity for intervention before more advanced symptoms develop.



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