



Alzheimer's Disease (AD) Is a Looming Healthcare Crisis

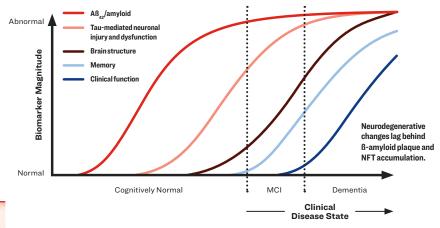
- AD is a progressive neurodegenerative disorder known to impact cognition, function, and behavior¹
- Exposure to various factors throughout life can increase one's risk for developing AD²
- Globally, AD is estimated to affect 22% of people aged 50 years and older³
- In the United States, the projected prevalence of AD dementia is expected to almost double between 2025 and 2060⁴

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AD Is Defined by Neuropathology^{1,5}

- AD is characterized by two abnormal protein aggregates:
 - Extracellular beta amyloid plaques
 - Intracellular neurofibrillary tangles containing hyperphosphorylated tau
- These protein accumulations contribute to neurodegeneration

AD pathology is thought to begin ~20 years before clinical symptoms^{1,5,6}



Hypothetical model of biomarkers of the AD pathological cascade, beginning with the abnormal accumulation of amyloid and the subsequent accumulation of tau, which leads to MCI and eventually dementia. Modified from Jack CR Jr, et al.⁶



The AD Continuum Consists of 6 Progressive Stages⁷

The stages range from asymptomatic to severe dementia. Note that neuropathology is present at each of these stages of AD.

Stage 1	
Preclinical AD	Pi
No	
impairment	n

Stage 2 Preclinical AD

Performs in normal range on cognitive tests. May experience subjective changes in cognition or changes in mood

Stage 3

AD With MCI

cognition.
Complex
ADLs may
be difficult.
Independence
is maintained

Stage 4

AD With Mild Dementia

Progressive cognitive and mild functional impairment on instrumental ADLs

Stage 5

AD With Moderate Dementia

Progressive cognitive and moderate functional impairment on basic ADLs requiring assistance

Stage 6

AD With Severe Dementia

Progressive cognitive and functional impairment. Complete dependence for basic ADLs

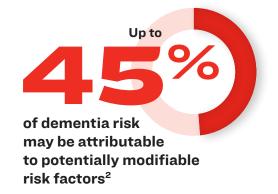






Opportunities for Impact: Potentially Modifiable Risk Factors

- While nonmodifiable risk factors such as age, family history, and genetics contribute to the risk of Alzheimer's disease (AD),⁸ up to 45% of dementia risk may be attributable to modifiable factors,² such as:
 - Education level
 - · Physical activity
 - Hearing loss
 - · Conditions such as hypertension, obesity, and diabetes
- To mitigate patient risk, consider:9-12
 - Counseling patients on brain health and dementia risk starting in midlife
 - Employing tools to identify at-risk patients (eg, CAIDE risk score)
 - Applying multidomain intervention strategies





Risk Reduction Recommendations¹⁰

For clinicians to address brain health and prevent cognitive decline in patients aged 45 years and older.



Neurovascular Risk Management

Manage hypertension or diabetes according to guidelines



Physical Activity

Assess annually; develop a plan that fits with the patient's lifestyle



Sleep

Assess quantity/ quality; encourage 7-8 hrs daily (including naps)



Nutrition

Assess annually; counsel on value of a healthy diet



Social Activity

Assess annually or after major life events; suggest strategies for enhancing social connection



Cognitive Stimulation

Ask patients about cognitive activity; provide suggestions as needed

Learn more about cognitive health at: medical.lilly.com/us/diseases/cognitivehealth

CAIDE=Cardiovascular Risk Factors, Aging and Incidence of Dementia

1. Porsteinsson AP, et al. *J Prev Alzheimers Dis.* 2021;8:371-386. 2. Livingston G, et al. *Lancet*. 2024;404(10452):572-628. 3. Gustavsson A, et al. *Alzheimers Dement*. 2023;19:658-670. 4. Rajan KB, et al. *Alzheimers Dement*. 2021;17:1966-1975. 5. Aisen PS, et al. *Alzheimers Res Ther*. 2017;9(1):1-10. 6. Jack CR Jr, et al. *Lancet Neurol*. 2013;12(2):207-216. 7. Jack CR Jr, et al. *Alzheimers Dement*. 2024;20(8):5143-5169. 8. Alzheimer's Association. *Alzheimers Dement*. 2024;20(5)3708-3821. 9. Visser LNC, et al. *Alzheimers Res Ther*. 2021;13:170. 10. Sabbagh MN, et al. *Alzheimers Dement*. 2022;18(8):1569-1579. 11. Solomon A, et al. Alzheimers Res Ther. 2021;13:171. 12. Ngandu T, et al. *Lancet*. 2015;385(9984):2255-2263.

