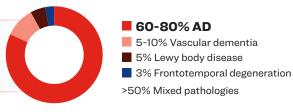
## **ALZHEIMER'S DISEASE (AD) FUNDAMENTALS**

### The Hidden Pathological **Progression of AD**

AD is a progressive neurodegenerative disorder that is thought to begin with the aberrant accumulation of amyloid plaques and neurofibrillary tangles (NFTs) in the brain, ultimately leading to cell death and increasingly debilitating cognitive, functional, and behavioral impairments.2

AD is the most common type of dementia. shown by percentage distribution of cases.1





### AD Exists Along a Progressive Continuum<sup>2-4</sup>

Stage

Genetically determined AD



Asymptomatic, deterministic gene



No evidence of

**Stages** 1-2

**Preclinical** AD

Normal performance within expected range on objective cognitive tests

Potential subjective cognitive decline or change in mood, anxiety. or motivation not explained

by life events (Stage 2)

Remains fully olo independent with no or minimal (Stage 2) functional impact on activities of daily living (ADLs)

Stage

3

Mild cognitive impairment (MCI) due to AD

Stage

Mild dementia due to AD

Stage 5

**Moderate** dementia due to AD

Stage

Severe dementia due to AD

range on objective cognitive tests independently.

Performs ADLs independently but functional impact on complex ADLs may be detectable

Performance in

the impaired/abnormal

Progressive cognitive and mild functional impairment on instrumental ADLs. with independence on basic ADLs

Progressive cognitive and moderate functional impairment on basic ADLs requiring assistance

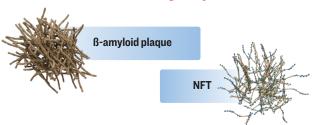
Progressive cognitive and functional impairment, and complete dependence for basic ADLs

Neuropathological changes in AD are present in all stages from Stage 1 to Stage 6.

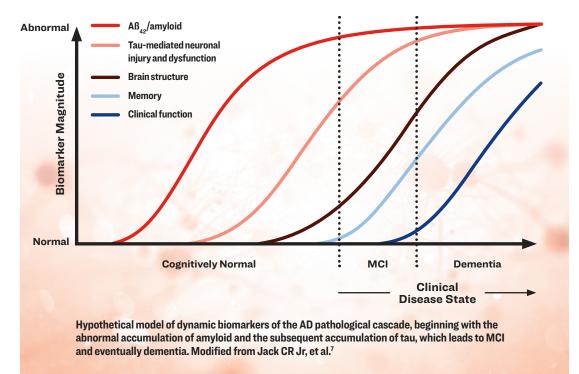
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## The Neuropathologic Changes of AD May Begin ~20 Years Before Clinical Symptoms<sup>2,4-7</sup>

Two primary hallmark neuropathologies characterize AD: extracellular ß-amyloid plaques comprised of amyloid beta peptides, and intracellular neurofibrillary tangles (NFTs) comprised of aggregated hyperphosphorylated tau protein.<sup>6</sup>



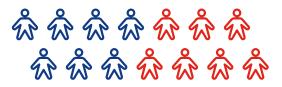
As the disease stages progress, neurodegenerative changes lag behind  $\beta$ -amyloid plaque and NFT accumulation.





The prevalence of AD dementia in adults aged 65 years and older is projected to double in the United States by 2060.<sup>1</sup>

~6.9 million in 2024¹ 
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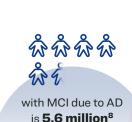


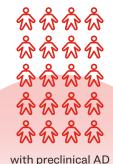
~14 million in 20601



#### Today millions more people are in the early stages of AD.

The estimated number of people in the United States aged 50 and older





is 20 million8

Explore AD's hidden story and learn more at: medical.lilly.com/us/diseases/cognitivehealth

1. Alzheimer's Association. *Alzheimers Dement*. 2024;20(5):3708-3821. 2. Porsteinsson AP, et al. *J Prev Alzheimers Dis*. 2021;8(3):371-386. 3. Jack CR, et al. *Alzheimers Dement*. 2018;14(4):535-562. 4. Jack CR Jr, et al. *Alzheimers Dement*. 2024;20(8):5143-5169. 5. McDade E, et al. *Alzheimers Dement* (N Y). 2020;6(1):1-9. 6. Aisen PS, et al. *Alzheimers Res Ther*. 2017;9(1):60. 7. Jack CR Jr, et al. *Lancet Neurol*. 2013;12(2):207-216. 8. Gustavsson A, et al. *Alzheimer's Dement*. 2023;19:658-670.

