You already know how important it is to discuss brain health and modifiable risk factors for cognitive decline with your patients. By taking simple, proactive steps, you can help many patients delay or prevent dementia. And the sooner you start talking about brain health and addressing modifiable risk factors the better, because the first symptoms often appear long after neurological changes begin. But how do you distinguish normal cognitive aging from dementia? What are clinical symptoms of cognitive decline and dementia, and how do these conditions progress over time? Let's break it down.

The differences between normal age-related cognitive changes and cognitive changes associated with Alzheimer's disease can be subtle. For example, normal aging is associated with occasional lapses in memory, such as forgetting names but remembering them later. On the other hand, memory changes related to Alzheimer's disease include persistent memory loss, such as forgetting recently learned information or asking the same questions repeatedly. The ability to complete familiar tasks can also differentiate normal aging from dementia due to Alzheimer's disease. In normal aging, individuals may occasionally need help with a device or appliance. In contrast, Alzheimer's disease often results in significant difficulty using appliances and devices, or in getting lost while driving to familiar places. Understanding these differences can help you provide clarity and reassurance to patients and families.

It's also important to know that the progression of symptoms related to the neurological changes of Alzheimer's disease follows a defined trajectory. In the preclinical stage, which can span many years, individuals don't exhibit symptoms but demonstrate measurable brain changes and biomarkers of Alzheimer's disease. In mild cognitive impairment, or MCI, due to Alzheimer's disease, cognitive decline becomes detectable but doesn't interfere with daily activities or overall functioning. In contrast, dementia due to Alzheimer's disease presents with impairments in memory, language, thinking, and behavior that disrupt a person's ability to function in daily life and worsen over time. So, Alzheimer's disease ultimately deprives patients of the ability to perform even the simplest tasks.

So, beyond discussing brain health and addressing modifiable risk factors, is there more you can do? Yes! Being aware of symptoms and the differences between normal aging and dementia enables earlier diagnosis. For even earlier detection, the neurological changes of Alzheimer's disease can be identified before clinical symptoms appear.

You are probably familiar with long-standing Alzheimer's disease biomarkers and tests used to detect them. Levels of beta-amyloid and tau can be measured in cerebrospinal fluid or through positron emission tomography, or PET, scans. Magnetic resonance imaging, or MRI, can detect degeneration in the brain. However, imaging tests are often expensive and may not be easily accessible, and many individuals may be hesitant to undergo a spinal tap for cerebrospinal fluid collection. In addition, current clinical use of biomarkers is primarily intended for symptomatic patients rather than cognitively unimpaired individuals.

This may soon change, however. Blood-based biomarkers may soon be available for routine clinical use. In fact, a blood test for tau demonstrates sensitivity and specificity comparable to FDA-approved tests that measure tau in cerebrospinal fluid. And, compared with cerebrospinal fluid and PET scans, blood-based biomarker tests are more scalable, cost-effective, and accessible, making them a promising option for broader implementation across clinical settings.

Of course, although some individuals may want to know whether they have biomarkers associated with Alzheimer's disease, others may prefer not to. As blood-based biomarkers approach clinical use, it is essential to consider the potential impact of a positive test on both the patient and their family. So, to

navigate these decisions effectively, it will be imperative to use a shared decision-making process. Explore how the patient would feel about knowing their risk for dementia. Find out how the test results might influence long-term decisions. Understand their values and what matters most to them, and address any concerns they may have. Give your patients and their families the best information you can so they can make an informed choice. And during these discussions, bear in mind that earlier diagnosis has large benefits for patients and their families. For patients, early diagnosis provides opportunities for:

- Earlier intervention, including potential anti-amyloid disease-modifying therapies
- Participation in clinical trials
- A longer period of independence
- Greater involvement in care decisions and
- Proactive management of legal and financial considerations

For families, early diagnosis allows more , me to adjust to changes in the pae nt's funcon, mood, and personality, and even reduces anxiety and depression. In fact, studies show that approximately 90% of individuals with demen, a prefer to receive a diagnosis as early as possible, and perceived delays in diagnosis are associated with sadness, anger, and despair among family members.

Timely diagnosis is possible! You can make a difference by knowing the cogniv e changes associated with demen, a and how they differ from normal aging; recognizing the progression of symptoms; inves, ga, ng biomarkers when appropriate; and preparing for the availability of blood tests in roune pracce . Don't delay! Detect cogniv e decline and Alzheimer's disease early and give your pae nts and their families the gi` of , me!

References

Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cogni, ve impairment due to Alzheimer's disease: recommendaons from the Naonal Instut e on Aging – Alzheimer's Associa, on workgroups on diagnosc guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7(3):270-279.

Alzheimer's Associa, on. Alzheimer's Disease Facts and Figures 2024. Available at h ps://www.alz.org/alzheimers-demena/f acts-figures. Accessed July 9, 2024.

Atri A. The Alzheimer's disease clinical spectrum: diagnosis and management. *Med Clin N Am*. 2019;103:263-293.

Barthélemy NR, Salvadó G, Schindler SE, et al. Highly accurate blood test for Alzheimer's disease is similar or superior to clinical cerebrospinal fluid tests. *Nat Med*. 2024;30:1085-1095.

Budson AE, Solomon PR. New diagnosc criteria for Alzheimer's disease and mild cogniv e impairment for the prac, cal neurologist. *Pract Neurol*. 2012;12(2):88-96.

Dubois B, Padovani A, Scheltens P, Rossi A, Dell' Agnello G. Timely diagnosis for Alzheimer's disease: a literature review on benefits and challenges. *J Alzheimer's Dis*. 2016;49(3):617-631.

Dubois B, Villain N, Frisoni GB, et al. Clinical diagnosis of Alzheimer's disease: recommendaon of the Interna, onal Working Group. *Lancet Neurol*. 2021;20(6):484-496.

Provided by the Academy for Continued Healthcare Learning (ACHL).
Supported by an educational grant from Lilly.

Halminen O, Vesikansa A, Mehtälä J, et al. Early start of an, -demena medicaon delays transion to 24-hour care in Alzheimer's disease pae nts: a Finnish naon wide cohort study. *J Alzheimers Dis*. 2021;81(3):1103-1115.

Jack CR, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Associa, on Workgroup. *Alzheimers Dement*. 2024;20(8):5143-5169.

Livingston G, Huntley J, Liu KY, et al. Demen, a preven, on, interven, on, and care: 2024 report of the *Lancet* standing Commission. *Lancet*. 2024;404:572-628.

McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of demen, a due to Alzheimer's disease: recommenda, ons from the Na, onal Ins, tute on Aging – Alzheimer's Associa, on workgroups on diagnosc guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7(3):263-269.

Mielke MM, Anderson M, Ashford JW, et al. Considera, ons for widespread implementa, on of blood-based biomarkers of Alzheimer's disease. *Alzheimers Dement*. 2024. doi: 10.1002/alz.14150. Online ahead of print.

Mielke MM, Anderson M, Ashford JW, et al. Recommenda, ons for clinical implementa, on of blood-based biomarkers for Alzheimer's disease. *Alzheimers Dement*. 2024. doi: 10.1002/alz.14184. Online ahead of print.

Palmqvist S, Tideman P, Mai sson-Carlgren N, et al. Blood biomarkers to detect Alzheimer disease in primary care and secondary care. *JAMA*. 2024;332(15):1245-1257.

Rasmussen J, Langerman H. Alzheimer's disease – why we need early diagnosis. *Degener Neurol Neuromuscul Dis*. 2019;9:123-130.

Sperling RA, Aisen PS, Beckei LA, et al. Toward defining the preclinical stages of Alzheimer's disease: recommenda, ons from the Na, onal Ins, tute on Aging – Alzheimer's Associa, on workgroups on diagnosc guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7(3):280-292.

Sperling RA, Donohue MC, Raman R, et al. Associa, on of factors with elevated amyloid burden in clinically normal older individuals. *JAMA Neurol*. 2020;77(6):735-745.

VandeVrede L, Rabinovici GD. Blood-based biomarkers for Alzheimer disease – ready for primary care? *JAMA Neurol*. 2024;81(10):1030-1031.

Wollney EN, Armstrong MJ, Bedenfield N, et al. Barriers and best prac, ces in disclosing a demen, a diagnosis: a clinician interview study. *Health Serv Insights*. 2022;15:11786329221141829.

Woods B, Arosio F, Diaz A, et al. Timely diagnosis of demen, a? Family carers' experiences in 5 European countries. *Int J Geriatr Psychiatry*. 2019;34(1):114-121.

ACHL
ACADEMY for CONTINUED HEALTHCARE LEARNING

Provided by the Academy for Continued Healthcare Learning (ACHL).
Supported by an educational grant from Lilly.