Early Detection of Alzheimer's Disease and Related Dementias:

GUIDANCE ON SHARED DECISION MAKING

Primary care physicians play a critical role in the care of patients with cognitive impairment and dementia, including patients with Alzheimer's disease and related dementias, or ADRD. Early diagnosis and management of ADRD requires a comprehensive, person-centered approach that integrates medical expertise with compassion, cultural sensitivity and a focus on individualized care.

The American Academy of Family Physicians designed this tool to provide primary care physicians with practical, evidence-based guidance to do the following:

- Support patients presenting with subjective cognitive concerns or abnormal cognitive assessments
- Navigate the diagnostic process for mild cognitive impairment, mild dementia and moderate dementia syndromes
- Tailor conversations to each patient's unique needs, emphasizing the goal of maintaining autonomy and independence while highlighting the importance of shared decision making in achieving those outcomes

Why Early Detection of ADRD Matters

- Patients with Alzheimer's disease are often misdiagnosed or diagnosed late in the disease course.[1-3]
- Early detection may improve adherence and clinical management of other chronic conditions in older adults.[4,5]
- Nonpharmacologic treatments, including lifestyle modifications, can improve cognitive function and increase the amount of time patients with ADRD live in the community.[6,7]
- Early detection can prevent financial abuse and enhance patient autonomy and independence.[8,9]
- For patients with cognitive impairment, medical evaluation of their impairment, differentiation of cognitive impairment stage and stratification for treatment can frequently be done in a primary care setting.

STEP 1 BEGIN THE CONVERSATION

- **Normalize aging and cognitive changes.** Describe normal age-related cognitive changes, such as occasionally forgetting names, misplacing items or forgetting why you walked into a room.
- **Explore subjective cognitive concerns.** Ask about changes your patient has noticed in their thinking or memory. For example, you could say, *"Your brain health is important, and I would like to know more about any concerns you have."* Have them compare their current memory to how it was in the past. Additionally, ask whether other people have noticed any cognitive changes in them.
- **Assess the impact of cognitive changes on daily life.** Ask how cognitive concerns are affecting your patient's ability to carry out day-to-day activities. Identify any challenges they have functioning at work, engaging in hobbies or maintaining independence. For example, you could ask, *"How have changes in your thinking or memory impacted the activities you do on a regular basis? Are there things you don't do anymore because of these changes?"*
- **Evaluate potential contributing factors and your patient's insights.** Discuss the potential role of reversible factors (e.g., medications, stress, depression, sleep disturbance, sensory deficits) that can affect cognition. Explore your patient's perspective on possible causes of their symptoms. Document any relevant family history of cognitive conditions (e.g., dementia).

STEP 2 HIGHLIGHT THE VALUE OF EARLY DETECTION AND DIAGNOSIS OF ADRD

- **Focus on the importance of early diagnosis.** Explain that detecting and diagnosing ADRD early makes it possible to plan and intervene before significant functional decline occurs. It may be easier for your patient to understand the role of proactive brain health assessment if you liken it to a familiar primary care model, such as monitoring and treating hypertension or diabetes. For example, you could say, *"Doing a cognitive assessment to check your brain health is similar to checking your blood pressure to monitor your heart health. In both cases,*

finding changes as early as possible can give us the opportunity to develop a treatment and care plan that fits your needs, preferences and goals."

- **Educate your patient on the benefits of lifestyle modifications for brain health.** For example, you could say, *"Daily actions such as making healthy diet choices, exercising, doing brain-stimulating puzzles, improving sleep habits and increasing social interaction have been shown to improve brain function and thinking, even in people who have early changes in their brain."* Some patients may have misconceptions about the lack of treatment options for ADRD. You can alleviate these by explaining that lifestyle modifications may help people with cognitive impairment live independently at home longer.
- **Explain that new drug treatment options are available.** Inform your patient that when treatment with these drugs is implemented early, they may slow disease progression by impacting the AD-related changes in the brain.

STEP 3 SET EXPECTATIONS FOR COGNITIVE ASSESSMENT AND DIAGNOSTIC EVALUATION[10]

- **Explain what a cognitive assessment involves.** Describe how a formal, office-based cognitive assessment can help determine the extent of any changes in cognition and functional status. If your patient has not already had blood and imaging tests to rule out other causes of cognitive changes, explain that these tests are the first step of the assessment. Additionally, let them know that you will assess reversible factors that can affect cognition, including the following:
  - Prescription medications and over-the-counter medications and supplements: As a person ages, medications they have taken for years can affect cognition and may need to be reduced or changed. OTC medications and supplements can also significantly impair cognition.
  - Mental health conditions: Common conditions like depression can lead to perceived short-term memory problems.
- **Explain what a diagnostic evaluation involves.** Emphasize that there are a number of conditions that can affect brain function, and many of them can be treated to improve symptoms. Explain that a diagnostic evaluation involves screening or testing for other conditions and then developing a management and/or treatment strategy for any conditions that are identified.
- **Conduct a cognitive assessment and diagnostic evaluation.**[10,11] All patients with subjective cognitive concerns should undergo an office-based cognitive assessment (e.g., Mini-Cog, Saint Louis University Mental Status [SLUMS], Mini-Mental State Exam [MMSE], Montreal Cognitive Assessment [MoCA]) and receive brain health education. Patients with positive results should undergo diagnostic evaluation for treatable and underlying causes. Additionally, conducting a functional assessment will allow you to differentiate between mild cognitive impairment and dementia.
- **Discuss genetic testing.** Patients may inquire about genetic testing, particularly regarding the apolipoprotein E 4 allele, which is associated with an increased risk of AD.[12] It is important to clarify the following:
  - The presence of the APOE4 allele does not determine AD development, and people without it can still develop AD.
  - Genetic testing is not a standard part of the diagnostic evaluation for cognitive symptoms because it does not change treatment or management.
  - Patients who are being considered for amyloid-targeting treatment (e.g., disease-modifying therapies) should undergo APOE4 testing to assess the risk of side effects, including amyloid-related imaging abnormalities, or ARIA.[13]

AAFP members can find more information on cognitive assessment and ADRD diagnostic evaluation in the *FP Essentials*™ edition on dementia.

Use of Blood Biomarkers in Primary Care

Testing for blood biomarkers, or BBMs, for Alzheimer's disease is a promising tool for early AD detection in primary care, especially given the limited access to dementia specialists.[13] This testing helps assess risk for AD in patients with cognitive impairment, evaluate response to treatment and improve patient selection for clinical trials. Phosphorylated tau 217 (p-tau217) and its combination with plasma amyloid-beta 42/40 are currently the most predictive plasma biomarkers for assessing amyloid and tau burden in the brain.[14-16]

Currently, BBM testing is most effectively used in primary care for patients with abnormal cognitive assessments, patients for whom other causes of cognitive impairment have been ruled out and patients who may be candidates for disease-modifying

therapies or other AD-specific treatments. It is important to note that experts do not recommend use of BBM testing in people who do not have cognitive impairment, as it can introduce diagnostic uncertainty.[13] Research continues to advance this field rapidly, and the clinical utility of BBMs may evolve as new evidence emerges.

When to Discuss Blood Biomarkers for AD

When laboratory testing, imaging and medical evaluations do not clearly identify the cause of a patient's measurable cognitive impairment, consider discussing blood biomarkers for AD. These biomarkers can provide additional insights into the underlying cause of changes in brain health, enhancing diagnostic accuracy. *Table 1* outlines key points to address when explaining BBM testing to patients.

Table 1. Key Points About BBM Testing for Patient Conversations

Role of BBM testing	Explain that BBM testing does not confirm a diagnosis, but it can help you reach a diagnosis sooner by assessing your patient's risk for AD as a cause of their cognitive changes. Emphasize that, like all tests, BBM testing has both benefits and limitations.	*"This blood test will help us better understand whether or not Alzheimer's disease is likely to be a cause for the symptoms you're experiencing. Although this test can't tell us for sure one way or the other, it can help us reach a diagnosis sooner."*
Benefits of BBM testing	Before testing, explain that one of the benefits of BBM testing is that it can help determine whether AD is likely contributing to your patient's cognitive difficulties. Having this information can clarify treatment options and guide care planning. If your patient's BBM test results are negative, the likelihood that AD is causing their cognitive difficulties is low. This makes identifying and treating other potential causes even more critical for their brain health. If their BBM test results are positive, it is more likely that AD is a significant factor in their cognitive symptoms. This information helps you determine which treatment options may be the most beneficial to explore. Keep in mind that results of BBM testing must always be interpreted in the context of a patient's overall health and symptoms.	*"One benefit of this blood test is that if the results are negative, we know that Alzheimer's disease is probably not the cause of the changes you're experiencing. This information allows us to focus on other ways to keep your brain healthy and improve your symptoms.* *If the test results are positive, we can work together to explore treatment options and plan appropriately for your care sooner."*
Risks of BBM testing	It is important to discuss potential risks of BBM testing with your patient. One consideration is that BBM test results become a part of their medical record and may potentially impact their ability to obtain some types of insurance. In addition, most health insurance does not cover BBM testing for AD at this time. Explain that no test is 100% accurate. BBMs can be impacted by a number of factors (e.g., medications, other chronic medical conditions). It is recommended that patients get further evaluation and additional testing to confirm their diagnosis.	*"One risk associated with this blood test is that the results will be part of your medical record. A positive test result might make it hard for you to do things like get long-term care insurance. Another thing to consider is that your health insurance may not cover the cost of this test."*

AD = Alzheimer's disease; BBM = blood biomarker.
Information from references 13, 17 and 18.

STEP 4 INTRODUCE EMERGING DISEASE-MODIFYING THERAPIES

A disease-modifying therapy for AD is defined as "an intervention that produces an enduring change in the clinical progression of AD by interfering in the underlying pathophysiological mechanisms of the disease process leading to cell death."[19] While the emerging benefits of DMTs are promising, discussing the potential risks with patients is important as well. Referring patients to be evaluated for DMTs may be appropriate for some patients with mild cognitive impairment or early dementia who are interested in exploring these therapies as a treatment option. Consider discussing a possible referral for DMT evaluation with patients who[20]:

- Have mild cognitive impairment or mild dementia syndrome
- Have mild/moderate vascular disease burden on imaging
- Are not on anticoagulants
- Do not have autoimmune conditions
- Have positive BBM test results

As trusted medical advisors, primary care physicians should discuss the risks and benefits of DMTs with patients and their caregivers to help them make informed decisions. You play a critical role in assessing a patient's eligibility for DMTs and confirming their eligibility with a local specialist, such as a neurologist or geriatrician. By facilitating rapid referrals for treatment, you can help maximize the potential benefits of DMTs for your patients.

Early Diagnosis Is Key in Emerging Treatments for AD

While opinions vary on the importance of DMTs for AD, advancements in pharmaceutical research are promising, with new treatments continually emerging. Since DMTs carry the lowest risk in patients with early cognitive changes, it is increasingly important for primary care physicians to facilitate early detection and diagnosis of AD. The combination of early detection and diagnosis, nonpharmacologic treatments and new pharmacologic treatments offers opportunities to improve patient outcomes.

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