Working Together:

Improving Early Diagngosis and Management of Alzheimer's Disease in Primary Care

New Jersey Academy of Family Physicians

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General Objective:
To leverage team-based care and the chronic care model to improve the use of assessment tools for early diagnosis of Alzheimer's disease (AD) and engage patients and their caregivers in the treatment plan.

Specific Objectives:
At the end of this activity learners will be able to:

- Explain the importance of early diagnosis of AD;
- Apply office-based cognitive assessment tools to aid in early diagnosis of AD;
- Employ an inter-disciplinary team in the management of behavioral issues in patients with AD;
- Engage in dialogue with patients and caregivers in a subsequent treatment plan.
- Outline a plan to connect patients with AD to community-based resources for long-term management.

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INTRODUCTION:

The Impact of Alzheimer's Disease (AD)

First reported in the early 20th Century, Alzheimer's disease (AD) is a progressive and fatal disorder characterized by hallmark protein changes and neuronal degeneration in the brain. Although individuals with early-stage AD may carry out daily activities with minimal assistance, the disease ultimately affects multiple areas of the brain, necessitating caregivers to help the patient sustain basic functions. AD accounts for 60%-80% of cases of dementia, as represented by difficulties with memory, language, problem-solving, and thinking.[1] The neuronal damage of AD eventually affects brain regions that support walking and swallowing, rendering the patient in need of constant care.

Alzheimer's dementia currently affects an estimated 6.5 million (10.7%) US adults ages 65 and older, a number that is projected to rise to 12.7 million by 2050 due to the aging of the US population.[2] Although incidence increases with age,[1] AD can manifest at any time, and the physiologic changes that underpin AD likely begin several decades before the patient notices symptoms.[3,4] Women account for approximately two-thirds of AD cases diagnosed in the US,[2] and analysis of Framingham Heart Study data suggests that women have a 1 in 5 lifetime risk for Alzheimer's dementia at age 45, compared to 1 in 10 for men.[5] Older non-Hispanic black people and Hispanic-Americans are disproportionately more likely than older white people to have Alzheimer's or other dementias,[1] more likely reflecting health and socioeconomic disparities than genetic distinctions.[6]

Alzheimer's disease exerts a formidable impact, both economically and on the families/caregivers of afflicted individuals. The rate of disease progression varies widely, with an average lifespan of 8 to 12 years from initial diagnosis.[1] A patient with Alzheimer's dementia requires increasingly encompassing care, complicating a measure of the total economic burden of AD. However, the Alzheimer's Association has estimated that, in addition to the economic costs of hired care, friends and family acting as caregivers provided more than $271 billion dollars in unpaid care to individuals with Alzheimer's and other dementias in 2021.[1] Prior to COVID-19, AD was the fifth-leading cause of death among individuals ages 65 and older in the US and a leading cause of disability and morbidity.[7] The impact of COVID-19 on AD morbidity, mortality, and caregiving remains to be determined, but Alzheimer's disease will unquestionably continue to be a major healthcare burden in the US.

Proactively screening for and diagnosing AD will enable patients and caregivers to develop an effective management plan, and many patients who experience symptoms of cognitive decline will initially visit their primary care clinician for treatment. To address the management of AD in primary care, the New Jersey Academy of Family Physicians (NJAFP) assembled a panel of experts to improve patient outcomes by increasing primary care clinicians' recognition of AD signs and symptoms and their comfort level with its initial and ongoing management. To achieve these aims, this publication reviews current literature and guidelines and provides recommendations to lower barriers to care and management of patients who present with AD risk factors or symptoms.

At-A-Glance

- Primary care clinicians play critical roles in identifying patients who have or are at risk for cognitive decline associated with Alzheimer's disease (AD) and ensuring that they receive prompt and effective care.
- Alzheimer's disease progresses along a continuum that spans three basic phases: pre-clinical AD; mild cognitive impairment (MCI) due to AD; and Alzheimer's dementia.
- Hallmark symptoms of early-stage AD include difficulty remembering recent conversations, names, or events, apathy, or depression.
- Early signs and symptoms of AD can often be distinguished from natural age-related cognitive changes.
- Early identification and proactive management of mild cognitive impairment can improve the quality of life for patients who will ultimately experience cognitive decline and for their caregivers.
- Many convenient screening tools for cognitive impairment can be implemented in primary care.
- Effective management requires honest and frank conversations, and the clinician should educate and prepare the patient and caregivers about what to expect.
- Several recently approved agents address the underlying biology of AD, although these are not widely available at present.
- Optimal management incorporates a holistic approach that combines medical, social, and emotional support for the patient and the caregiver.
- Management includes establishing a professional AD care team (e.g., neurologist, gerontologist, social worker, psychiatrist) and ensuring that family care-givers receive effective training in managing the day-to-day life of the care recipient.

Alzheimer's Disease: The Most Common Cause of Dementia

Alzheimer's disease is the most common cause of dementia, a term that describes a group of neurologic conditions that are characterized by difficulties with memory, language, problem-solving, and other thinking skills.[1] Dementias are not part of the normal aging process; they are caused by specific changes in the brain and are usually degenerative in nature. While this monograph focuses on AD, many patients who are diagnosed with the condition will ask, "How do you know that it's AD?" Numerous types of dementia have been characterized, but four types—AD, frontotemporal dementia, Lewy body dementia, and vascular dementia—account for the vast majority of cases. Table 1 summarizes salient characteristics of these common dementias.[8] It should be noted that an individual may concomitantly show symptoms and/or pathologic evidence of more than one type of dementia, a designation known as *mixed dementia* or *mixed etiology dementia*.

TABLE 1. Common Types of Dementia[8]

Type	Brain Abnormalities	Symptoms	Typical Age at Diagnosis
Alzheimer's Disease	Deposits of ß-amyloid protein and tangles of tau protein throughout brain	• Impaired memory, language, visual/spatial skills • Apathy • Depression	65+; some cases mid-30s to early 60s
Frontotemporal Dementia	Accumulation of tau and TDP-43 proteins in neurons in the frontal and temporal lobes	• Personality changes • Issues with language • Blance issues; palsy • Lack of emotional/impulse control	45-64
Lewy Body Dementia	Deposits of alpha-synuclein protein ("Lewy bodies") on cortical nerve cells	• Hallucinations • Sleep difficulties • Impaired thinking and motor skills • Inability to concentrate or maintain attention	50 and older
Vascular Dementia	Disrupted blood flow to the brain (e.g., stroke, vascular disease)	• Impaired motor skills and judgement • Memory issues • Hallucinations/delusions	Over 65

The Pathophysiology of AD

Alzheimer's disease is characterized by two prototypical lesions in the brain: 1) senile plaques, or extracellular lesions composed of accumulated insoluble β-amyloid peptide (Aβ), and 2) intra-neuronal fibrous tangles (NFT) of hyperphosphorylated tau protein (P-tau).[9] β-amyloid protein can also be deposited within the walls of capillaries and blood vessels, thus compromising blood flow and causing additional cerebral angiopathy.[9] Several mechanisms have been proposed to explain the relationship between these changes and cognitive decline. The central tenet is that the protein deposits excessively stimulate neurotransmitter receptors in the neuronal membranes, ultimately promoting a collapse in calcium homeostasis, inflammation, and the depletion of energy and neuronal factors.[9,10] This process damages neurons and synapses involved in memory, learning, and other cognitive functions. The long-standing "amyloid cascade theory" postulates that the accumulation of the Aβ peptide is the causative factor for the observed changes, including the NFT of tau protein.[11,12] Tau protein functions primarily in microtubule synthesis and stabilization. Hyperphosphorylation results in loss of function, promoting neuronal damage and leading to cytotoxicity.[13]

The Alzheimer's Disease Continuum

Alzheimer's disease progresses along a continuum that spans three basic phases: 1) pre-clinical AD; 2) mild cognitive impairment (MCI) due to AD; and 3) Alzheimer's dementia.[1] An individual's duration in each phase is influenced by multiple factors, including sex, clinical setting, the presence of abnormal tau protein, and evidence of carrying the APOE ε4 allele.[14]

Pre-clinical Phase. Patients in the pre-clinical phase have biomarker evidence of the brain changes that predate cognitive impairment, as measured by PET scan or analysis of serum or cerebrospinal fluid. At this point, the brain can compensate for the damage due to neuronal loss, and the patient is asymptomatic. Although most will ultimately experience cognitive impairment, some individuals who have Alzheimer's-related brain changes do not develop the hallmark symptoms of MCI or Alzheimer's dementia.

MCI Due to Alzheimer's Disease. This phase is characterized by a combination of biomarker evidence of brain changes plus subtle symptoms, such as issues with memory, language, or thinking. The emergence of symptoms indicates that the brain is no longer able to compensate fully for the degree of neuron loss and damage. Although noticeable to the affected individual and their close contacts, these symptoms do not necessarily impair daily activities. MCI prevalence increases with age, affecting an estimated 6.7% of individuals aged 60-64 and 25.2% of those aged 80-84.[15] Approximately 15% of individuals with MCI aged 65 and older develop dementia after two years, although some individuals never progress beyond MCI.[15]

Dementia Due to Alzheimer's Disease. This stage spans a range of symptom severity (mild, moderate, and severe) that differs from MCI in that the changes impair daily function. Whereas individuals with mild Alzheimer's dementia may be able to drive or continue working, those with moderate dementia often have difficulty completing multistep tasks such as getting dressed, may experience personality changes, and may have difficulty recognizing loved ones. Severe Alzheimer's dementia is characterized by an inability to communicate, and, as movement becomes impaired, a bed-bound state.

Risk Factors for Developing AD

Risk factors for AD can be genetic or acquired, and the condition cannot be prevented per se. However, some "protective measures" can potentially influence the onset or rate of cognitive decline. The next two sections will review the key inherent and modifiable risk factors for Alzheimer's dementia and suggest potential ways to reduce the risk of developing disease.

AD is characterized as early-onset, in which symptoms appear before

age 65 (4%-6% of AD cases), or late-onset, in which symptoms manifest at age 65 or older. Beyond age of presentation, these two forms can also be distinguished on the basis of various clinical, psychosocial, and neuropathologic variables and genetic risk factors.[16]

Genetic Risk Factors. Genetic factors account for an estimated 70% of the risk for developing AD,[17] and a number of susceptibility genes and polymorphisms have been linked with disease. These aberrations are nearly always associated with processes implicated in the formation or deposition of Aβ plaques. Early-onset disease has been associated with mutations in presenilin 1 (PSEN1), presenilin 2 (PSEN2), or amyloid precursor protein (APP), whereas late-onset AD is primarily associated with the presence of the ε4 allele in the apolipoprotein E gene (APOE).[9,17] APOE protein binds soluble Aβ, directly influencing its clearance or accumulation. APOE ε4 alleles accelerate Aβ deposition and profoundly increase the risk of developing AD from three-fold (one APOE ε4 allele) to twelve-fold (two alleles).[16]

Acquired Risk Factors. Several acquired factors have also been associated with increased risk for AD based on physiologic mechanisms or data from epidemiologic analyses (Table 2).[9] The most commonly reported factor, cerebrovascular disease (e.g., hemorrhagic infarcts, cortical infarcts, vasculopathies), shares many risk factors with AD. These conditions can compromise the integrity of the blood-brain barrier, ultimately damaging neurons by reducing the cerebral blood supply and promoting the buildup of neurotoxic molecules such as Aβ and tau peptides. Other AD risk factors (e.g., hypertension, hypercholesterolemia, type 2 diabetes, obesity, smoking) negatively impact vasculature and can either promote the synthesis of or reduce the clearance of Aβ. It should be noted that multiple mechanisms have been proposed to explain AD's association with these multifactorial conditions. Managing these risk factors is a central tenet of a healthy lifestyle that confers a secondary benefit of reducing the risk for dementia.

In animal models of AD, stress hyper-activates the hypothalamic, pituitary, and adrenal axis, increasing cortisol production and promoting Aβ peptide deposition in the hypothalamus and prefrontal cortex[18] and the accumulation of hyperphosphorylated tau protein.[19] Patients with AD have demonstrated increased cortisol levels relative to controls in some studies.[9] The literature also suggests that early-life depression, i.e., in the pre-clinical stages of dementia, may presage dementia later in life. Early onset of depression and its duration and frequency have been associated with up to a four-fold increased risk of developing dementia.[20] Moreover, a recent meta-analysis of the relationship between sleep and cognitive impairment found that individuals who self-reported sleep disturbances had a higher risk of all-cause dementia, AD, and vascular dementia than those who reported no sleep disturbances.[21] Meta-analyses and cohort studies have also identified widowhood as a risk factor for AD and other forms of dementia. One study that assessed midlife relationship status and cognitive function later in life found that people without a partner had a two-fold risk of developing cognitive impairment and AD compared to those who lived with a partner.[22]

TABLE 2. Acquired Risk Factors for Alzheimer's Disease[9]

- Cerebrovascualr disease
- Diabetes
- Hypertension
- Obesity
- Hypercholesterolemia
- Marital status (widowhood)
- Stress
- Depression
- Inadequate sleep/sleep disturbances
- Smoking

Measures to Reduce the Risk of Cognitive Decline

Cognitive Reserve. An established body of literature supports the concept that measures taken throughout life to increase "cognitive reserve," or the capacity to tolerate age- or disease-related changes in the brain without developing clinical symptoms, can help to maintain cognitive function and postpone clinical dementia and AD.[23,24] Cognitive reserve can be built through mentally stimulating patterns of behavior (e.g., formal education, lifestyle pursuits, occupational complexity, a mentally and socially integrated lifestyle) across the age continuum. Physical activity likely plays a role as well, and it has been postulated that leisure activities that meld physical, mental, and social stimulation have the most beneficial effect.[24] It should be noted that cognitive reserve can be enhanced at any stage of life through many accessible activities—solving crossword puzzles, playing a musical instrument, participating in a book club, or taking a routine walk with a friend may pay hidden dividends at a later stage.

Physical Activity. Data from several meta-analyses suggest that higher levels of physical activity are associated with a reduced risk of cognitive decline and dementia.[25,26] Physical activity can lower blood pressure, improve lipid profiles, help regulate glycemic levels, and facilitate weight management, thus impacting many of the acquired risk factors of AD. Furthermore, physical activity is postulated to exert brain-specific effects that could prevent AD, including increasing neurotrophic factors, reducing free radicals in the hippocampus, and stimulating neurogenesis and synaptic plasticity, among others.[9] The Expert Panel recommends encouraging patients who present with or are at risk for cognitive impairment to be active within appropriate contexts, with a particular focus on incorporating aerobic activity. A successful activity regimen will be tailored to the patient's needs and should utilize available resources. Physical activity/exercise is optimally structured through an exercise or rehabilitation specialist, such as a physical therapist.

Diet and Supplements. Meta-analyses have indicated that, compared to age-matched controls, individuals with AD have significantly lower CSF/brain levels of docosahexaenoic acid (DHA), choline-containing lipids, folate, vitamin B_{12}, vitamin C, and vitamin E.[27] Furthermore, antioxidants, fatty acids, and B vitamins have been linked with better cognitive functioning in prospective epidemiologic studies, although the value of any specific nutrient has not been confirmed in randomized clinical trials.[28] While there is no "magic bullet" dietary supplement to counteract cognitive decline, certain foods may naturally help to prevent it. Patients may ask about the Dietary Approaches to Stop Hypertension (DASH) or "Mediterranean" diets, which are frequently linked to longevity and health in popular information sources. These diets are rich in whole foods (e.g., fruits, vegetables, fish, nuts, beans, olive oil) but low in pro-

cessed foods and saturated fats. Foods commonly included in these diets can lower blood pressure, protect against chronic conditions, reduce inflammation, and support weight loss regimens. While detailed dietary recommendations are beyond the scope of this monograph, general guidelines are available online.[29,30] Given that these diets aim to counteract many acquired risk factors for AD, the Expert Panel endorses them as part of a healthy lifestyle that may positively impact cognitive decline. When possible, the Panel suggests partnering with a clinical nutritionist or dietitian to work with the patient to tailor a healthy diet.

Patients may also inquire about the efficacy of popular "brain health" supplements (e.g., apoaequorin) that propose to boost memory or enhance brain function. These products have been marketed aggressively but are not supported by any clinical evidence to date. The Expert Panel does not recommend these products for individuals who are concerned about memory loss.

Other Considerations. Vitamin B_{12} deficiency has been associated with symptoms similar to those observed with cognitive decline (e.g., memory loss, confusion).[31] As part of a differential diagnosis, the Expert Panel recommends measuring B_{12} level in patients who have signs of or are at risk for cognitive impairment and supplementing as needed. Other hormones, such as vitamin D and estrogen, have been linked epidemiologically with risk of developing AD.[9] However, inconsistent findings and a lack of randomized trial evidence argue against using these agents to target cognitive decline. As with vitamin B_{12}, vitamin D deficiency should be screened and supplemented (especially in elderly patients), given its central role in calcium metabolism and bone regulation.

"Where Did I Put my Keys?": Is it Early-stage Alzheimer's Dementia or Typical Age-related Cognitive Change?

The AD continuum reflects a progressive and irreversible loss of cognitive function resulting from neuronal damage. However, the brain undergoes normal age-related cognitive changes, and adult life is rife with stimuli. The brain processes and filters a vast amount of information when determining where to focus attention. At some point, everyone struggles to remember the name of a recent acquaintance or to recall where they placed their phone or keys, and an isolated instance of forgetting an account password does not in itself constitute a warning sign of dementia. The differences between normal age-related change and early signs of dementia can be subtle, and some non-dementia conditions may present with dementia-like symptoms (Table 3).

TABLE 3. Non-dementia Conditions that may present with Dementialike Symptoms[1]

- Depression
- Sleep apnea
- Delirium
- Medication side effects
- Lyme disease
- Vitamin B_{12} deficiency
- Excessive alcohol consumption

Hallmark symptoms of early-stage AD include difficulty remembering recent conversations, names, or events, apathy, or depression. In many instances, the patient's spouse or a family member may report that their loved one is struggling with short-term memory, requiring that interchanges be repeated for comprehension. Some patients may actively deny this development even though it is happening. To help tease out subtle differences and aid in early diagnosis, the Alzheimer's Association has created a list of the 10 Early Signs and Symptoms of Alzheimer's Disease and how they contrast with typical age-related changes (Table 4).[1]

The Role of the Primary Care Clinician

Primary care clinicians play critical roles in identifying patients who have or are at risk for AD and ensuring that they receive prompt and effective care.

The primary care physician should communicate with patients who have signs of cognitive decline and support those who require additional assessment and ongoing services. Additional roles of the clinician include:

- Identifying patients at risk for AD or other cognitive disorders
- Understanding cultural factors and patient preferences for treatment
- Discussing practical considerations for managing cognitive impairment
- Discussing treatment options and adjunctive interventions with the patient and caregivers
- Coordinating efforts with an AD care team (e.g., neurologist, gerontologist, social worker)
- Keeping the patient actively engaged in disease management

Given that many patients may be uncomfortable when receiving a diagnosis of dementia, the primary care clinician must recognize that he or she provides key support to help the individual receive proper treatment.

Early Detection of Cognitive Impairment in Primary Care

Because AD is characterized by brain lesions, definitive diagnosis is usually established through autopsy by the presence of Aβ plaques and tau protein tangles. However, early identification and proactive management of mild cognitive impairment can improve the quality of life for patients who will ultimately experience cognitive decline and for their caregivers. Early diagnosis provides the family and other caregivers with an improved understanding of a patient's behavioral changes and enables early treatment to maintain daily functioning and slow cognitive decline. To this end, the American Academy of Neurology has issued evidence-based recommendations for assessing cognitive impairment (Table 5).[15] As noted in the table, cognitive assessment for signs of dementia is included in the Annual "Wellness" Visits covered by Medicare Part B,[32] and the Alzheimer's Association has developed a Cognitive Assessment Toolkit to help physicians detect cognitive impairment during the Medicare Annual Wellness Visit.[33] Cognitive assessment toolkits are also available from the American Academy of Family Physicians[34] and ACT on Alzheimer's.[35] It should also be noted that the US Preventive Services Task Force (USPSTF) has recently concluded that the current evidence is insufficient to assess the balance of benefits and harms of screening for cognitive impairment in asymptomatic, community-dwelling adults ages 65 and older.[36]

TABLE 4. Ten Early Signs and Symptoms of AD[1]

Sign	Examples of AD	Typical Age-related Change
Memory loss that disrupts daily life	• Forgetting recently learned information or important dates/events • Asking the same questions over and over • Increasingly relying on memory aids or family members for things previoulsy handled solo	Sometimes forgetting names or appointments but remembering them later
Challenges in planning or solving problems	• Difficulty developing a plan or working with numbers • Trouble following a familiar recipe or keeping track of monthly bills • Difficulty concentrating; taking much longer to do things than previously needed	Occasionally erring when managing finances or household bills
Difficulty completing familiar tasks	• Trouble driving to a familiar location or organizing a grocery list • Difficulty remembering the rules of a favorite game	Occasionally needing help to use microwave settings or to record a TV show
Confusion with time or place	• Losing track of dates, seasons, and passage of time • Trouble understanding something if not happening immediately • Forgetting where one is or how one arrived there	Getting confused about the day of the week but figuring it out later
Trouble understanding visual images and spatial relationships	• Vision problems that may lead to difficulty with balance or trouble reading • Problems judging distance and determining color or contrast, causing issues with driving	Vision changes related to cataracts
New problems with words when speaking or writing	• Trouble following or joining a conversation • Stopping in the middle of a conversation with no idea how to continue • Repeating one's own statements • Struggling with vocabulary • Having trouble naming a familiar object or using the wrong name (e.g., calling a "watch" a "hand-clock")	Sometimes having trouble finding the right word
Misplacing items and losing the ability to retrace steps	• Putting items in unusual places • Losing items and being unable to retrace their steps to locate them • Accusing others of stealing, especially as the disease progresses	Misplacing things from time to time and retracing steps to find them
Decreased or poor judgment	• Changes in judgement or decision-making • Using poor judgement when dealing with money • Paying less attention to grooming or keeping clean	Making a bad decision once in a while, like neglecting to change the oil in the car
Withdrawal from work or social activities	• Experience changes in the ability to hold or follow a conversation • Withdraw from hobbies, social activities, or other engagements • Have trouble keeping up with a favorite team or activity	Sometimes feeling uninterested in family or social obligations
Changes in mood or personality	• Experience mood and personality changes • Become confused, suspicious, de-pressed, fearful, or anxious • Be easily upset at home, with friends, or when out of a comfort zone	Developing very specific ways of doing things and becoming irritable when a routine is disrupted

Source: Alzheimer's Association. https://www.alz.org/alzheimers-dementia/10_signs. A worksheet version of this material is available at https://www.alz.org/media/Documents/alzheimers-dementia-10-signs-worksheet.pdf.

Initial cognitive evaluation in a medical setting establishes a baseline that can be followed over time to track changes. Primary care clinicians who suspect MCI in an affected patient have several informative detection tools (Table 6) that can be implemented in the office.

While these assessments provide insight into the type and severity of impairment, a diagnosis of dementia cannot be made solely on the basis of a low score on one of these tests. When assessing for cognitive impairment, screening tools must be evaluated within a holistic context that includes a physical examination, family history, medical history, and laboratory tests as needed to rule out conditions (e.g., vitamin B_{12} deficiency, hypothyroidism) that could produce symptoms

TABLE 5. American Academy of Neurology Practice Recommendation for Assessing for Mild Cognitive Impairment (MCI)[15]

Recommendation	Evidence Level*
For patients for whom the patient or a close contact voices con-cern about memory or impaired cognition, clinicians should as-sess for MCI and not assume the concerns are related to normal aging.	B
When performing a Medicare Annual Wellness Visit, clinicians should not rely on historical report of subjective memory con-cerns alone when assessing for cognitive impairment.	B
For patients for whom screening or as-sessing for MCI is appropriate, clinicians should use validated assessment tools. For patients who test positive for MCI, clini-cians should perform a more formal clinical assessment for diagnosis of MCI.	B
For patients with MCI, clinicians should assess for the presence of functional im-pairment related to cognition before giving a diagnosis of dementia.	B
For patients suspected to have MCI, clini-cians who lack the necessary experience should refer these patients to a specialist with experience in cognition.	B
For patients diagnosed with MCI, clinicians should perform a medical evaluation for MCI risk factors that are potentially modifi-able.	B
For patients diagnosed with MCI, clinicians should perform serial assessments over time to monitor for changes in cognitive status.	B
For patients and families asking about bio-markers in MCI, clinicians should counsel that there are no accepted biomarkers available at this time.	B

***Level B:** Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population.

TABLE 6. Detection Tools - Publicly Available Screening Instruments

Test / Screen	Site
Clock Drawing Test (CDT)	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5619351
Memory Impairment Screen	https://www.alz.org/media/documents/memory-impair-ment-screening-mis.pdf
MIS by Telephone (MIS-T)	https://pblob1storage.blob.core.windows.net/public/nadrc/docs/Memory-Im-pairment-Screen-tele-phone-(MIS-T)-508.pdf
Short Portable Mental Status Questionnaire (SPMSQ)	https://geriatrics.stanford.edu/culturemed/overview/assessment/assessment_toolkit/spmsq.html
Mini-Cog Verbal Fluency	https://mini-cog.com/
AD8 Dementia Screening Interview	https://www.alz.org/media/Documents/ad8-demen-tia-screening.pdf
Functional Activities Questionnaire (FAQ)	https://www.healthcare.uiowa.edu/familymedicine/fpinfo/docs/functional-activ-ities-assessment-tool.pdf
Abbreviated Mental Test (AMT-10)	https://www.parkinsons.va.gov/resources/MO-CA-Test-English.pdf
Montreal Cognitive Assessment (MoCA)*	https://www.parkinsons.va.gov/resources/MO-CA-Test-English.pdf
St. Louis University Mental Status Examination (SLUMS)*	https://www.slu.edu/medi-cine/internal-medicine/geri-atric-medicine/aging-suc-cessfully/assessment-tools/mental-status-exam.php
Telephone Instrument for Cognitive Status (TICS)	https://sites.cscc.unc.edu/aric/sites/default/files/pub-lic/forms/TIC.pdf
Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)	https://www.alz.org/media/documents/short-form-in-formant-questionnaire-de-cline.pdf

* Requires certification or training to administer

similar to those of dementia. It should be noted that the perspective of an informant who has a close relationship with the patient will often prove insightful.

There are no recommendations to support either the routine use of neuroimaging in patients with dementia or routine genetic testing for the APOE ε4 allele. Neuroimaging using CT or MRI is indicated, however, in patients who present with rapidly progressing dementia, measured in the scale of days to months.37 The acute onset of cognitive impairment, rapid neurologic degeneration, or findings suggestive of stroke, cerebral hemorrhage, or subdural hematoma warrant imaging and referral to a neurologist.

The Expert Panel recommends that all individuals under evaluation for MCI or AD be screened for depression, which can mimic dementia and worsen cognitive impairment when present. Validated screening tools such as the Patient Health Questionnaire-2 (PHQ-2; https://www.hiv.uw.edu/page/mental-health-screening/phq-2) and PHQ-9 (https://www.hiv.uw.edu/page/mental-health-screening/phq-9) can be administered in the office setting.

Proactive Management of AD

When a patient presents with symptoms that suggest cognitive decline, clear and thorough communication with the individual and their caregiver is paramount. Communicating with the patient about their symptoms and history will provide insight into the extent of impairment, comorbidities, risk factors, and potential exacerbating factors. While this information contextualizes the patient's current status, the person who hears that he or she may possibly develop dementia will most certainly be concerned about what lies ahead. Proactive management of dementias can improve the quality of life for affected individuals and their caregivers, and the Alzheimer's Association has identified nine components of active management (Table 7) that should be factored into all plans.[1]

The primary care clinician represents one member of a care team that must be assembled to help the patient and his/her caregivers manage the course of dementia. Professionals will include the primary care clinician, neurologist, counselors, and other specialists as needed (e.g., therapist, cardiologist). Lay members of the team will include a trusted decision-maker, family members and close friends, neighbors and others who can help with day-to-day tasks, and community/social service members. Caregivers may find it useful to join support groups and to have options for scheduled assistance. Primary care clinicians should be prepared to establish social services links as one component of management.

"What Will Happen to Me?": Talking with Your Patient and Their Caregivers about MCI and AD

Primary care clinicians are often the initial medical points of contact for individuals who present with signs of cognitive decline. Diagnosis and management of dementia mandate an ongoing conversation between patient and clinician. Many patients will be worried about AD based on family history or anecdotal experiences; others will harbor misperceptions about the condition and treatment options. The primary care clinician can set the stage for effective management by framing these early conversations so that the patient and caregiver feel empowered to move forward.

Effective management requires honest and frank conversations, and the clinician should educate and prepare the patient and caregivers about what to expect. Each patient is unique in their needs, and initial visits should aim to build a trusting relationship that will promote effective long-term management. The Expert Panel advocates that the clinician be straightforward and open about management challenges, addressing practical issues such as advanced directives (e.g., power of attorney, living wills, guardianship, end-of-life care/portable medical orders), the possibility of developing comorbidities such as anxiety or depression, and the behavioral changes that the afflicted individual may experience. For follow-up visits, the Expert Panel suggests that the patient and/or caregiver write down his/her questions before coming to the office so that no concern is overlooked. Evidence-based recommendations for managing MCI from the American Academy of Neurology are highlighted in Table 8.[15]

TABLE 7. Central Tenets of Proactive Management of AD and Other Dementias[1]

- Appropriate use of available treatment options
- Effective management of coexisting conditions
- Providing family caregivers with effective training in man aging the day-to-day life of the care recipient
- Coordination of care among physicians, other healthcare professionals, and lay caregivers
- Participation in activities that are meaningful to the individual with dementia and bring purpose to their life
- Maintaining a sense of self-identity and relationships with others
- Having opportunities to connect with others living with dementia, such as support groups and supportive services
- Becoming educated about the disease
- Planning for the future

TABLE 8. American Academy of Neurology Practice Recommendations for Managing Mild Cognitive Impairment (MCI)[15]

Recommendation	Evidence Level*
Clinicians should wean patients from medications that can contribute to cognitive impairment (where feasible and medically appropriate) and treat modifiable risk factors that may be contributing.†	B
Clinicians should recommend regular exercise (twice/week) as part of an overall approach to management.	B
Clinicians should discuss diagnosis and uncertainties regarding prognosis. Clinicians should counsel patients and families to discuss long-term planning topics such as advance directives, driving safety, finances, and estate planning.	B
Clinicians should assess for behavioral and neuropsychiatric symptoms and treat with both pharmacologic and non-pharma cologic approaches when indicated.	B
Clinicians may recommend cognitive interventions.	C

***Level B:** Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population.
Level C: Possibly effective, ineffective, or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population.

†Medications with side effects that can affect thinking include benzodiazepines, anticholinergics, antihistamines, opioids, and proton pump inhibitors.

When having these conversations, the clinician should also note that each individual's progress through this continuum is unique. Many individuals live well for years with Alzheimer's disease, and it is impossible to assign a timeframe for upcoming developments. A diagnosis of cognitive impairment does not automatically signal a death sentence, and conversations should focus on maintaining quality of life during this journey.

Treating AD and Lessening Its Symptoms

The neuronal damage associated with MCI is irreversible, making early diagnosis and prompt treatment the cornerstones of successful management and improving quality of life for the patient and caregivers. Optimal management incorporates a holistic approach that combines medical, social, and emotional support. As noted in previous sections, lifestyle modifications can be beneficial. Although there is no cure for Alzheimer's dementia, patients and their caregivers will likely ask about available medications. This section will review potentially appropriate FDA-approved pharmacotherapies that can be implemented in primary care.

Pharmacotherapy. FDA-approved pharmacotherapies that may apply to patients with AD fall within two general categories: 1) treatments that address the underlying disease biology and 2) medications that may help lessen symptoms (e.g., memory loss, confusion).

Treatments that Address the Underlying Disease Biology. In 2021 and 2023, the US FDA used its Accelerated Approval Pathway to approve the monoclonal antibodies aducanumab and lecanemab to treat patients with mild cognitive impairment or mild dementia due to Alzheimer's disease.[38,39] Because of the accelerated approvals, no safety or efficacy data are currently available to support initiating treatment at earlier or later stages of disease.[40] These agents target beta-amyloid protein isoforms that can form plaques, thereby decreasing (but not halting) Aβ production. Although there is no evidence that these agents restore lost memories or cognitive function, the lessening of Aβ plaque accumulation in the brain reduces cognitive and functional decline in individuals who have early-stage AD.[41,42] While there is no specific diagnostic test required to initiate these agents, the presence of Aβ plaques should be confirmed before prescribing. There are no contraindications for use, although precautions for amyloid-related imaging abnormalities and infusion-related reactions are noted.[38,39]

Despite promising results, these agents' approvals have been controversial, and their use as treatments for AD continues to be debated based on safety and efficacy concerns and cost.[43,44] With the FDA approval of lecanemab, CMS has stated that they will cover the medication. Coverage for aducanumab was approved in 2022. Coverage by private insurers varies. At present, there are no head-to-head comparison studies of the two agents.

Medications that May Help Lessen AD Symptoms. The FDA has approved certain cholinesterase inhibitors and glutamate regulators to treat symptoms related to memory, language, and other thought processes (Table 9). Cholinesterase inhibitors prevent the breakdown of acetylcholine, thereby enhancing communication between neurons. These agents appear to be equally efficacious, and it is not possible to identify responders upfront.[45] Side effects from these agents are generally mild and may include nausea, vomiting, loss of appetite, and increased frequency of bowel movements. One glutamate regulator, memantine, has been approved to improve memory, attention, reason, language, and the ability to perform simple tasks. Side effects include headache, constipation, confusion, and dizziness. Donepezil plus memantine is also available as a combined agent.

The FDA has also approved suvorexant to treat insomnia, and the agent has been shown effective as a sleep aid in persons with mild to moderate AD.[46] Side effects include impaired alertness and motor coordination, worsening of depression or suicidal ideation, complex sleep behaviors or sleep paralysis, and compromised respiratory function.

It should be stressed that none of the agents that may lessen symptoms slows the progression of cognitive decline. Studies of cholinesterase inhibitors in individuals with MCI showed no benefit on cognitive outcomes or reduction in progression from MCI to dementia.[15] To this end, the American Academy of Neurology has issued the following recommendations about prescribing cholinesterase inhibitors to patients with MCI:[15]

- For patients diagnosed with MCI, clinicians may choose not to offer cholinesterase inhibitors. (Evidence Level: B)
- If clinicians choose to offer cholinesterase inhibitors [to patients with MCI], they must first discuss with patients the fact that this is an off-label prescription not currently backed by empirical evi dence. (Evidence Level: A)

TABLE 9. FDA-approved Medications that May Help Lessen AD Symptoms

Category	Agents	Indications
Cholinesterase inhibitors	Donepezil	Mild to severe AD[47]
	Galantamine	Mild to moderate AD[48]
	Rivastigmine	• Mild to moderate AD[49] • Mild to moderate dementia associated with Parkinson's disease
Glutamate regulators	Memantine	Moderate to severe AD[50]
Combined agents	Memantine + donepezil	Moderate to severe AD[51]
Orexin antagonists	Suvorexant	Insomnia[52]

Clinical Trial Participation

The treatment landscape for AD continues to evolve, and some patients may be willing to participate in a clinical trial to receive new treatments and advance the state of understanding for the disease. Several agencies offer clinical trial matching services that may be of interest to some patients and their caregivers (Table 10).

Providing Culturally Informed Care to the Minority Patient with Cognitive Decline

Why Being Culturally Informed Is Important. Being culturally informed extends beyond simply being thoughtful or politically correct; it has become a necessary component of contemporary medical practice in the US. According to 2022 estimates from the US Census Bureau, people of color (Latinos, African-Americans, Asians, Pacific Islanders, and American Indian/Alaskan Natives) make up nearly one-third of the US population.[53] Data from 2017-2021 indicate that 21.7% of the US population speaks a language other than English at home, and an estimated 13.6% of the US population is foreign-born.[53] Because of the increasing need for medical personnel to interact with persons from diverse cultural backgrounds, governing bodies of medical schools (e.g., the Liaison Committee on Medical Education) and residency programs (the Accreditation Council for Graduate Medical Education) require that cultural competence be included in medical school and residency curricula. In addition, several states have enacted laws or mandates requiring practicing physicians to have continuing medical education in cultural competency to maintain licensure.

Cultural Beliefs and Norms Shape Attitudes toward Illness and Medical Treatment. Attitudes toward illness and medical treatment are influenced by cultural beliefs and norms. A primary care practice will serve patients whose cultural norms vary widely with respect to disease causation, acceptable forms of treatment, spiritual beliefs, and family structure and member roles— factors that can impact the management of cognitive impairment or AD. While it is impossible to understand the nuances of every cultural milieu that will be encountered in primary health care, the clinician must be informed of patterns and trends in cultural beliefs to communicate effectively with minority populations commonly encountered in a culturally diverse practice.

Establishing a Culturally Informed Office Environment. Establishing a culturally informed office environment is the first step toward providing culturally appropriate care. Patients within specific ethnic groups may exhibit substantial differences in the degree of their sensitivities toward prevailing American culture. For example, recent African immigrants may exhibit cultural sensitivities that differ widely from those seen in American-born black patients, and Spanish-speaking patients may represent the diverse cultural backgrounds of their home countries (e.g., Guatemala, Mexico, Nicaragua). Components of a culturally informed office include the appropriate physical environment (e.g., language- and topic-appropriate magazines for adults, books and toys appropriate to children, a staff to match the patient population served, and bilingual or language-appropriate wall posters and signs). Reading capacity should be evaluated in cases where language barriers or health literacy barriers may pose communication issues. To facilitate comprehension, it is recommended that written text be geared toward a 6th-grade reading level or below. Interpretation services should also be made available; per federal law (enforced through the US Office of Civil Rights), the healthcare clinician's office must provide a trained medical interpreter. The "teach-back" approach asking the patient to explain the plan and instructions back to you will help assure that vital information is not misunderstood. Staff should also be trained in a culturally informed manner to overcome assumptions about, or bias against, particular cultural backgrounds.

It should be noted that a culturally appropriate and validated cognitive screening tool may not be readily available for every patient. If formal screening is impractical, clinical history and informant input can inform a diagnosis of dementia, especially in the context of how the patient's function has changed related to daily abilities.[35] Cognitive evaluation is an opportunity for ongoing monitoring, and screens can be re-implemented as needed to assess changes.

Partnering with the Minority Patient. Appreciating the value system imposed by cultural heritage is necessary to begin a conversation with a patient who presents with symptoms of cognitive decline. Minority patients may respond to a holistic biopsychosocial approach that emphasizes patient care by recognizing biological, psychological, and spiritual components. Such an approach encourages an ongoing, active partnership between the patient and the physician in which treatment is structured to account for the patient's value system. Patients must be given a framework to understand their condition that takes into account the level of disease severity and realistic treatment options. Communicating effectively with a given patient depends to an extent on the individual and his/her relationship with the clinician. Nonetheless, an engaged attitude is central to a success-

TABLE 10. Clinical Trials matching Resources

Agency	Program	Contact Information
Alzheimer's Association	TrialMatch	https://www.alz.org/alzheimers-dementia/research_progress/clinical-trials/trialmatch 1-800-272-3900
National Institute on Aging	Alzheimer's and Related Dementias Education & Referral (ADEAR) Center	https://www.alzheimers.gov/clinical-trials 1-800-438-4380
National Institutes of Health	Clinicaltrials.gov	https://www.alzheimers.gov/clinical-trials 1-800-438-4380
Mayo Clinic		https://www.mayo.edu/research/clinical-trials/search-results?studySiteStatusesGrouped=Open/Status%20Unknown&pocId=CON-20205683

ful relationship. Showing the patient that you care promotes trust; invoking a paternalistic approach may create a barrier to providing appropriate care.

Culturally informed care is based on a partnership between the patient and the healthcare clinician.

Considerations for Delivering Culturally Informed Care to Latino Patients.[54] While the assessment of treatment needs of Latinos varies somewhat according to population subgroup, this section will summarize several key considerations and strategies to provide effective, appropriate care to Latino patients.

Cultural beliefs toward illness shape many aspects of the interaction between the Latino patient and the clinician, and cultural idioms may surface during conversation. For example, illness may be perceived as the result of an imbalance between external and internal sources (e.g., hot and cold, body and soul). The clinician should recognize that some Latinos remain strongly grounded in the folk-healing traditions of their home cultures; patients may have sought the assistance of a curandero (folk healer) to alleviate symptoms. Furthermore, the process of acculturation may also lead some Latino patients to define certain diseases using folk idioms (e.g., empacho for indigestion) while characterizing others according to Western medical criteria (e.g., measles, asthma).

TABLE 11. Memory Loss Resources for Clinicians and Patients

Source	Contact	Resources
Alzheimer's Association	www.alz.org 1-800-272-3900	• Education center • Patient information resources
National Institute on Aging	www.nia.nih.gov/alzheimers 1-800-438-4380	• Information for clinicians, • families, and caregivers • Referrals to local and national resources
National Institute of Neurological Disorders and Stroke	www.ninds.nih.gov 1-800-352-9424	• Multilingual resources • Patient information • Clnical trials information
Alzheimer's Foundation of America	www.alzfdn.org 1-866-232-8484	• Patient information • Webinars for caregivers • Online memory screening / tests
Caring.com	https://www.caring.com/senior-living/memory-care-facilities/ 1-800-973-1540	• Assisted living locator • Caregiver resources

Moreover, the clinician must pay careful attention to accommodate the support systems that may serve the ailing Latino patient. For example, spiritual belief may play a central role in treatment. A Latino patient may believe that God determines the outcome of the treatment or course of disease; for example, nervios (a cultural concept of distress evoked by difficult life circumstances) may result from insufficient prayer or from God failing to hear the patient's supplications. A broad base of potential counseling sources may be appropriate for minority patients; if a Latino patient is amenable to working with clergy or a social worker, this option should be incorporated into the management plan. The clinician should also recognize the central role of the family (familismo) as a source of emotional support during treatment processes. Therefore, the clinician should engage the family in discussions that involve decisions about care, recognizing also that family members may draw upon their own spirituality to cope with a relative's illness. The influence of social and spiritual support suggests that clinicians must access the local world of their patients and their families to provide culturally responsive care to Latino patients.

Considerations for Delivering Culturally Informed Care to African-American Patients. Disparities in AD diagnosis and treatment in African-Americans are multifactorial and can include financial barriers, feelings of mistrust, and perceptions of racism or discrimination. Among these are issues with physician communication style, masking of disease by somatic presentation of symptoms or self-medication, and concerns about the stigma of illness. Respectful behavior and a demonstrated willingness to listen and communicate can aid in building trust with African-American patients. To foster communication, the healthcare clinician should:

- Respect the patient's understanding of his/her illness
- Use open-ended questions to ensure that you and the patient have common meaning
- Recognize the medical beliefs of the patient, including folk-home-, and herbal-based remedies. This may require cross-cultural negotiation regarding treatment
- Recognize the role of spirituality as a coping mechanism
- Incorporate beneficial or neutral folk remedies into the plan of care
- Recognize that medication cost and complex dosage instructions may promote non-adherence

When to Refer to a Neurologist

Diagnosing and treating uncomplicated dementia falls well within the scope of family medicine. However, some patients may present complications that necessitate referral to a neurologist at some point in the treatment continuum. Situations that warrant referral include:

- Patients under age 65 who present with memory loss or cognitive changes
- Patients with acute or rapidly progressing cognitive impairment;
- Patients with findings suggestive of stroke, cerebral hemorrhage, or subdural hematoma
- Case-specific factors, including complicated or atypical presentation, symptoms, or disease progression
- Other reasons at the discretion of the primary care clinician.

AD Resources for Clinicians and Patients

The AD community includes many online support groups, help services, blogs, and resources that may be useful for patients with

cognitive impairment and their caregivers to connect with others. Table 11 lists resources that provide a broad range of AD-related information and can serve as launching points for clinicians and patients who seek information about diagnosing, managing, and caring for someone with memory loss and/or Alzheimer's disease.

Additional Reading

Screening for Cognitive Impairment in Older Adults: US Preventive Services Task Force Recommendation Statement [Link to: https://jamanetwork.com/journals/jama/fullarticle/2761651]

CMS: Cognitive Assessment & Care Plan Services [https://www.cms.gov/cognitive]

Anti-Amyloid Monoclonal Antibodies are Transformative Treatments that Redefine Alzheimer's Disease Therapeutics [https://link.springer.com/article/10.1007/s40265-023-01858-9]

Balancing the Conflicting Goals for Treatment of Alzheimer's Disease with Monoclonal Antibodies [https://link.springer.com/article/10.14283/jpad.2023.71]

Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer's Disease CED Study Registry [https://qualitynet.cms.gov/alzheimers-ced-registry]

CONCLUSION

Alzheimer's disease is a progressive disorder characterized by two prototypical brain lesions: 1) senile plaques, or extracellular lesions composed of accumulated insoluble β-amyloid peptide (Aβ), and 2) intra-neuronal fibrous tangles (NFT) of hyperphosphorylated tau protein (P-tau). Alzheimer's disease progresses along a continuum that spans pre-clinical AD, MCI due to AD, and Alzheimer's dementia. An individual's duration in each phase is influenced by multiple factors, including sex, clinical setting, the presence of abnormal tau protein, and evidence of carrying the APOE ε4 allele. Hallmark symptoms of early-stage AD include difficulty remembering recent conversations, names, or events, apathy, or depression.

Proactively screening for and diagnosing AD will enable patients and caregivers to develop an effective management plan. Early identification and proactive management of MCI can improve the quality of life for patients who will ultimately experience cognitive decline and for their caregivers. Clinicians must engage the patient and their caregivers in frank, practical discussions about what to expect along the disease continuum. Management includes establishing an AD care team (e.g., neurologist, gerontologist, social worker, psychiatrist) and ensuring that family caregivers receive effective training in managing the day-to-day life of the care recipient. The treatment landscape for cognitive impairment is evolving, but there are no agents that can reverse cognitive decline that has already taken place. Optimal management that incorporates medical, social, and emotional support will ensure the best quality of life for the patient and his/her caregivers. Through prompt diagnosis and proactive management, the primary care clinician plays a vital role in improving the quality of life for patients who suffer from cognitive impairment.

CASE STUDIES

Lena: *Diagnosing AD*

Lena is a 65-year-old African-American woman who arrives at your office with her daughter and son-in-law, who state that Lena is having trouble remembering details about her home and sometimes loses track of who she is speaking to. Lena says that, although she sometimes forgets details, it is due to "just getting old and tired." Lena's daughter also notes that her mother has periods where she does not seem to be her usual self—although Lena is lucid some of the time, her daughter notes that she also has had multiple episodes where she appears to be in a mental fog, forgetting recent conversations and events. Her son-in-law states that he first noticed Lena's confusion about a year ago but that it has gradually evolved from an isolated instance or two to occur nearly every time he speaks with her. Lena lives alone, and her family is increasingly concerned for her daily welfare. With only this information, should you suspect cognitive impairment/early-stage AD?

a. Yes. Lena shows hallmark symptoms of early-stage AD, such as difficulty remembering recent conversations, names, or events. Her self-characterization as "old and tired" may also suggest depression, another AD-associated symptom and a risk factor.

b. No. Dementia is unlikely to affect an otherwise healthy 65-year-old, and sometimes forgetting names or appointments is typical, as long as they can be recalled at a later point.

Answer: a. Although this limited presentation does not confirm AD, Lena's short-term memory issues suggest cognitive impairment that could represent (or become) AD. AD symptoms can onset at any age.

Lena's blood pressure is 130/80 mm Hg, which is controlled with lisinopril. Her pulse is 78 beats/minute. Her physical exam is normal, and her BMI is 25 kg/m2. She does not drink or smoke and does not currently take any prescription medications beyond the ACE inhibitor. What other assessments can help you determine whether Lena's symptoms represent cognitive impairment?

a. A validated test of memory and cognitive function, such as the Mini-Mental State Examination (MMSE) or Montreal Cognitive Assessment (MoCA)
b. A depression screen, such as the PHQ-2 or PHQ-9
c. Family history
d. Laboratory tests as needed to rule out conditions (e.g., vitamin B12 deficiency, hypothyroidism) that could produce symptoms similar to those of dementia
e. All of the above

Answer: e. At this point, you should look to rule out any condition whose symptoms could mask as dementia and to gain a more nuanced sense of Lena's memory and cognitive functioning.

You administer the MMSE and PHQ-2 in the office. Lena's score on the former falls into the range of abnormal function. How can you interpret this result in the context of what you know so far?

a. Lena has cognitive impairment that extends beyond age-related change. The MMSE and other validated tests of memory and cognitive function can serve as definitive instruments to diagnose cognitive impairment in the presence of other symptoms.
b. Lena likely has cognitive impairment that extends beyond age-related change. There is no single test that will diagnose cogni tive impairment or AD unequivocally. However, a score below the threshold for normal cognition, when taken in the context of other information present, is suggestive of cognitive impairment.
c. The results of these screens are inconclusive.

Answer: b. Lena is likely experiencing some cognitive impairment, and proactive management is warranted.

What other tests should you order at this point that will help you to proceed?

a. Genetic testing for the APOE ε4 allele
b. Neuroimaging via MRI or CT
c. Routine lipid panel
d. Thyroid hormone panel
e. All of the above
f. c and d only

Answer: f. There are no recommendations to support either the routine use of neuroimaging in patients with MCI/dementia or routine genetic testing for the APOE ε4 allele. Lipid and thyroid function panels will provide baseline values and could indicate specific areas of management to address as part of an overall care plan.

Lena's impaired cognitive function is beginning to impact her daily life, and proactive management is warranted to maintain her quality of life and ensure that she receives needed assistance. Which of the following factors should you consider when working with the care team to develop a management plan?

a. Effectively managing coexisting conditions
b. Providing family caregivers with effective training in managing Lena's day-to-day life going forward
c. Coordinating care among physicians, other healthcare profes sionals, and lay caregivers
d. Using appropriate available treatment options
e. Educating Lena and her caregivers about cognitive impairment and AD
f. Planning for the future
g. Connecting the family with others living with dementia, such as support groups and supportive services
h. All of the above

Answer: h. All of these are tenets of a management program for persons who live with dementia and their caregivers.

Lena's daughter asks about a supplement that she saw on social media that is billed as a natural memory aid that boosts brain function. Would you recommend that Lena take this supplement?

a. No. "Memory aid" supplements have been marketed aggres sively but are not supported by any clinical evidence to date. There is no proof that such agents have any benefit on cognition.
b. Yes. These formulations are relatively harmless in that their components are natural products that can be found in various diets. There is no harm in trying one of these products, although it may or may not work.

Answer: a. The safety and efficacy of these agents have not been tested fully in clinical trials. They are not FDA-approved and could potentially be harmful.

Lena asks if there are any medicines that she can take to restore lost memory function. Which of the following FDA-approved agents can reverse neuronal damage, effectively restoring some lost cognitive function?

a. Aducanumab
b. Donepezil
c. Galantamine
d. Lecanemab
e. Rivastigmine
f. Memantine
g. a and d only
h. None of the above

Answer: h. The neuronal damage associated with MCI and/or AD is irreversible, making early diagnosis and prompt treatment the cornerstones of successful management and improving quality of life for the patient and caregivers.

You schedule a follow-up visit with Lena, her daughter, and her son-in-law in a week to discuss laboratory results and to establish a plan forward. What elements should you address in this conversation?

a. Practical issues such as advance directives (e.g., power of attor ney, living wills, driving issues, guardianship)
b. Comorbidities such as anxiety or depression
c. Planning for behavioral changes that Lena may experience
d. Uncertainties regarding prognosis and limitations of treatment options
e. All of the above

Answer: e. All of these topics must be discussed, frankly and upfront, with the patient and primary caregivers.

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