

FACULTY GUIDE

Core Module 2:

Diagnosing Dementia

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Slide 1:

- Module 2 addresses the definitions and criteria associated with dementia generally and Alzheimer's disease and related dementias (or ADRD) specifically. The module is targeted towards those providers who are instrumental in providing a diagnosis of dementia. We will focus predominantly on the respective criteria most commonly cited in the literature. We will also introduce and explain the changes included in the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (or DSM-5).

Slide 3:

- As you can see in the outline for Module 2, we begin globally by examining what dementia is and how to detect it in a primary care setting. We then focus on the detection and diagnosis of specific types of dementia.

Slide 4:

- Our goal, by the time we finish with this module, is for you to complete four learning objectives. You will be able to:
 - Recognize and discuss the benefits of early detection and diagnosis of dementia in a primary care setting.
 - Identify the differences between routine screening of persons in a primary care setting and assessing or diagnosing persons with a specific type of dementia.
 - Identify the diagnostic process associated with the most common types of dementia—Alzheimer's disease, vascular dementia, dementia with Lewy bodies, Parkinson's disease dementia, and frontotemporal degeneration.
 - Identify tools and tests that can be used in the diagnostic process, including their benefits and disadvantages.

Slide 5:

- Early detection of cognitive impairment using available brief assessments is an important first step in diagnosing dementia.
- Dementia is a group of symptoms and not a part of normal aging.
- Dementia is caused by many diseases and conditions affecting the brain:
 - The most common type of dementia is Alzheimer's disease, followed by vascular dementia, dementia with Lewy bodies (DLB), Parkinson's disease dementia (PDD), frontotemporal degeneration (FTD), and mixed dementia.
- Early diagnosis of dementia and underlying causes allows for appropriate medical management, access to resources and clinical trials, and future planning with input from the persons living with dementia.
- Use of biomarkers for Alzheimer's disease is an emerging field—brain amyloid PET scans are available with FDA-approved radioactive tracers.

Slide 6:

- We are going to begin by looking at what constitutes dementia. We will then proceed to examine the benefits of early detection, including how to integrate detection into the Medicare Annual Wellness Visit.
- We will then focus on the specifics of diagnosing dementia—including making a differential diagnosis among the 3D's (namely, dementia, delirium, and depression)—before moving on to the specific diagnostic processes for Alzheimer's disease and related dementias.

Slide 7:

- Dementia is an acquired clinical syndrome with many potential causes and etiologies that is not a normal part of aging. Once a person has been diagnosed with dementia, it is important to then determine the underlying etiology, or etiologies in the case of mixed dementia, because treatments differ by dementia type.
- The recently revised guidelines developed by the National Institute on Aging (or NIA) and the Alzheimer's Association (or AA) note that all-cause dementia can be diagnosed if a person has cognitive or behavioral symptoms that interfere with his or her ability to function at work or socially. These symptoms must represent a decline from the previous level of functioning and cannot be explained by delirium or a major psychiatric disorder.
- For a diagnosis of dementia, there must be evidence of impairments in at least two of the following domains:
 - The ability to acquire and recall new information
 - Reasoning and handling of complex tasks
 - Poor judgment (such as impairments in instrumental activities of daily living or IADL)
 - Visuospatial ability
 - Language function
 - Changes in personality, behavior, or comportment
- The guidelines note that the cognitive or behavioral impairments are detected through a combination of the (typically) older adult's history, (ideally obtained from both the older adult and a knowledgeable informant), and through cognitive assessments (McKhann et al., 2011).

Slide 9:

- Persons living with dementia (or PLwD) generally (but do not necessarily) manifest with memory impairment and one of the following:
 - Aphasia: A person can initiate and maintain a conversation but has impaired comprehension. There is intact grammar and syntax, but speech is vague, and the person often uses nonspecific phrases (such as "thing" instead of "cat").
 - Apraxia: A person is unable to carry out motor activities despite intact motor function; this contributes to loss of basic activities of daily living (ADLs).
 - Agnosia: A person is unable to recognize or identify objects despite intact sensory function; this typically appears later in the course of dementia and can be visual or tactile.

- Impaired executive function: A person has difficulty planning, initiating, sequencing, monitoring, or stopping complex behaviors; this appears during early- to middle-stage dementia and interferes with the ability to perform IADLs.
- Together, these deficits cause significant impairment in social or occupational functioning (Cooper & Greene, 2005).

Slide 10:

- In 2013, the most recent American Psychological Association's Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) replaced the category of "delirium, dementia, amnestic and other cognitive disorders" with the category of "neurocognitive disorders" (or NCD). These disorders have been subdivided into "mild" and "major" neurocognitive disorders.
- Mild neurocognitive disorders (or mNCD) represent a new subcategory that was derived from research on mild cognitive impairment. It is identified by a noticeable reduction in cognitive functioning that goes beyond the normal changes associated with aging and may or may not progress to dementia.
- Major neurocognitive disorders (or MNCD) now replaces "dementia" or other debilitating conditions.
- DSM-5 recognizes a wide range of subtypes of major neurocognitive disorders that must be coded when this diagnosis is made, including (but not limited to) Alzheimer's disease, vascular neurocognitive disorder (or vascular dementia), frontotemporal neurocognitive disorder (or frontotemporal degeneration), Lewy body dementias, Parkinson's disease, or HIV.
- For our purposes throughout these modules, we are using the terms mild cognitive impairment (MCI) instead of mild neurocognitive disorders and the specific subtypes of major neurocognitive disorders.

Slide 11:

- Now that we have a clear picture of the defining characteristics associated with a diagnosis of dementia, let's look at early detection and diagnosis.

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- As we will be discussing in greater detail in Module 4, dementia is a life-changing diagnosis.
- There are many benefits associated with early detection and diagnosis of dementia, both for persons living with dementia and their family and care partners.
- Once a diagnosis has been made, it is important for providers to explain to the person and family members that treatments do exist and that response to treatment varies, as does how the different types of dementia progress over time. It is important to emphasize, there is no cure for Alzheimer's disease and related dementias (ADRD). This information provides the family with meaningful information to help both the older adult and family plan for the future.
- There are numerous benefits associated with early detection. Early detection and diagnosis allows persons living with dementia to be involved in planning their future, while the person is still capable of making these decisions. These decisions may address medical considerations and health care directives, as well as issues regarding financial and legal planning. Early diagnosis may also help preserve the person's functioning longer through appropriate medical

management of other co-existing medical conditions. For example, it provides an opportunity to optimize the medical management of other conditions that could worsen cognition.

- It allows persons living with dementia and the family (or care partner) to build an appropriate interprofessional care team.
- Providers can connect persons and their care partners to appropriate community services and support systems. In addition, early diagnosis increases the opportunity for the persons living with dementia to become involved in clinical trials, if they so choose.
- There are also benefits to the care partners and family members. Early diagnosis can provide an explanation for the observed impairments. It enables the family to begin planning for the future, anticipate the various manifestations of progressive dementia, and connect to appropriate referrals and community services.
- There is a need to balance the pros and cons of screening asymptomatic persons for dementia. Currently, as will be discussed next, there is a difference of opinion regarding this—the U.S. Preventive Services Task Force (USPSTF) is reevaluating its recommendation, but the Medicare Annual Wellness Visit requires providers to assess for cognitive impairment.
- There is a need to determine whether the benefits of knowing about a diagnosis of dementia through routine screening outweigh the costs and risks associated with pursuing and obtaining the diagnosis.
- Currently, as we discuss next, there is insufficient evidence as to the benefits or harms associated with routine **screening** for cognitive impairment in older adults.

Slide 14:

- As mentioned, there is insufficient evidence as to the benefits or harms associated with screening for cognitive impairment in older adults. The United States Preventive Services Task Force (or USPSTF) released its recommendation regarding screening for cognitive impairment in asymptomatic older adults in 2014. The USPSTF concludes that the current evidence is “insufficient to assess the balance of benefits and harms of screening for cognitive impairment”.
- In explaining this recommendation, the USPSTF notes that this applies to universal screening with formal screening instruments of community-dwelling adults over age 65 who have no signs or symptoms of cognitive impairment.
- This recommendation does not apply to the early detection or diagnosis of dementia through the assessment of signs and symptoms that have been noted by persons living with dementia, their family members, or physicians or other providers. In fact, the USPSTF recognized that the use of cognitive assessment tools can increase detection of cognitive impairment but that they do not necessarily improve decision-making or influence outcomes.
- The USPSTF notes that “screening tests” include asking persons living with dementia to perform a series of tasks that assess one or more cognitive domains (such as memory, attention, language, and visuospatial or executive functioning).
- Brief instruments to screen for cognitive impairment can adequately detect cognitive impairment, but whether interventions for persons living with dementia or their care partners have a clinically significant effect in persons with earlier detected cognitive impairment is still unclear.

Slide 15:

- One of the new Medicare benefits added by the Centers for Medicare and Medicaid Services (or CMS) as part of the Affordable Care Act (or ACA) is the Annual Wellness Visit (or AWV). Providers are encouraged, but not required, to furnish AWVs to all of their Medicare patients. The AWV, including a cognitive assessment, can be performed by a physician, nurse practitioner, physician's assistant, clinical nurse specialist, or other health care professional working under the supervision of a physician. The AWV includes a requirement to assess for cognitive impairment, regardless of whether signs of dementia are present. As part of the Medicare AWV, the older adult must complete a Health Risk Assessment (or HRA), which could suggest cognitive impairment.
- Cognitive impairment can be detected by "assessment of an individual's cognitive function by direct observation, with due consideration of information obtained by way of patient report, concerns raised by family members, friends, caretakers, or others." There is no gold standard assessment tool that is appropriate for everyone. Nevertheless, the Alzheimer's Association and other organizations recommend using an objective tool.

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- A recent expert consensus panel was convened by the International Association of Gerontology and Geriatrics (or IAGG) and its Global Aging Research Network (or GARN) to identify means toward enhancing brain health. The panel noted the benefits of early recognition of cognitive impairment and supports the CMS findings for detecting cognitive impairment as part of the Medicare AWV, as well as the international call for early detection of cognitive impairment as an older adult's right.
- The panel noted that there are validated (screening) tests that take between 3 and 7 minutes to administer. These tests, when combined with patient- and informant-based screens, are the most appropriate approach for identifying early cognitive impairment.
- The IAGG panel noted that early cognitive impairment may have treatable components. For example, vitamin deficiencies and several endocrine concerns have been associated with cognitive impairment; however, while there is evidence that address some vitamin deficiencies may improve current cognition, there is no evidence that treating these issues will improve cognition or influence the possibility of future dementia. The panel also discussed emerging evidence that supports a combination of medical and lifestyle interventions as potential avenues for delaying or reducing cognitive decline.

Slide 17:

- We will switch gears now and begin to examine what is involved in making a diagnosis first of dementia and, then in the last segment, of specific types of dementia.

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- Dementia is an umbrella term, not a specific disease. "Dementia" encompasses a group of symptoms that affect cognitive abilities, executive functioning, and psychosocial abilities severely enough to interfere with daily functioning.

- Dementia is often undetected in the primary care setting. Persons living with dementia may not be aware of the presence, extent, or impact of their cognitive deficits and, therefore, may not raise these concerns with their primary care providers. Many persons living with early dementia may look and act otherwise healthy.
- Although universal screening is not recommended by the USPSTF, primary care providers should consider dementia in a differential diagnosis of all adult persons (of any age) who present with symptoms of memory difficulty that interferes with daily functioning, unexplained functional decline, or new onset psychiatric symptoms.
- Also, dementia should be considered in persons who have had deterioration in their personal hygiene or who suddenly have difficulty adhering to their medication regimens.

Slide 20:

- Primary care is often the first point of contact for persons living with dementia.
- Primary care providers have many roles, including:
 - Exclude potentially treatable illness or reversible cause of dementia
 - Evaluate, diagnose and manage dementia
 - Refer for specialist assessment
 - Monitor and provide follow-up
- Adults who manifest subjective signs and/or symptoms of cognitive impairment or dementia should undergo further evaluation.
- Screening typically involves a brief standardized objective instrument in conjunction with observation or information from the patient or a knowledgeable informant. This instrument can identify persons who demonstrate some degree of cognitive impairment.
- The use of a brief, structured cognitive assessment tool correctly classifies older adults as possibly having dementia or mild cognitive impairment (MCI) more often than detection by a patient's own primary care physician (83 percent vs. 59 percent, respectively). The results are often supported by a brief history from both the patient and an informant. However, a brief screen cannot diagnose dementia.

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- As we will be discussing over the next few slides, components of the diagnostic evaluation for dementia include:
- Observation for common warning signs
- Medical and symptom history (from patient and informant)
- Cognitive screening test
- Standard medical tests to rule out reversible causes of dementia or coexisting disorders
- Additional tests as warranted.

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- Primary care providers should note the following of all adult persons, even if their primary complaint is not related to cognition, as it could signify a decline in cognitive function:
 - Their behavior on arrival in office, including interactions with staff
 - Their ability or inability to keep track of a conversation

- Whether they have a propensity to repeat themselves and if there is change over time
- Whether they rely on their care partner to answer questions
- If they are wearing appropriate clothing and maintaining their personal hygiene
- Whether they have experienced excessive weight gain or loss over time.
- Whether there are any changes to gait or mood.
- Whether they have missed numerous appointments
- Other warning signs that might raise suspicion of dementia include indications that persons have forgotten how to do activities that were previously routine (such as cooking, playing cards, or making simple repairs), that they are losing their ability to perform instrumental activities of daily living (such as handling money or balancing a checkbook), misplacing household objects in unusual places (for example, car keys in the refrigerator), or getting lost in familiar surroundings.
- Indications that they are relying on someone else to help them make decisions or handle instrumental activities of daily living (IADLs) might also be a warning sign of dementia.

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- Dementia has a multifactorial etiology. Obtaining an in-depth history regarding the patient's symptoms helps a provider develop a differential diagnosis of dementia and begin determining the underlying etiology of the dementia.
- As discussed later in this module, and again in module 5, several types of information can help in the diagnosis of dementia and in the differential diagnosis of etiology (Simmons et al., 2011).
- Whether or not the symptoms are of concern to the older adult
- When the person first noticed the symptoms
- If and how the symptoms have changed over time
- How fast the symptoms have progressed
- Whether the symptoms interfere with daily activities, and, if so, in what ways
- Other pertinent information can help a provider develop a differential diagnosis:
 - Past and present history of any medical and psychiatric illness
 - The entire list of medications, vitamins, supplements, and herbal remedies the person is taking.
 - Any family history of dementia or psychiatric illness,
 - Any familial or personal vascular risk factors
 - Any recent or prior traumatic brain injury.

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- Other pertinent information can help a provider develop a differential diagnosis:
 - Any hallucinations or delusions, and if so:
 - What was the nature of the hallucinations or delusions?
 - Were they visual or auditory?
 - What was the content of the delusion?
 - Any history of Parkinsonism
 - Any history of alcohol or psychoactive drug abuse
 - Any recent changes in sleep patterns
 - Whether there have been any recent changes in mood
 - Any signs of loss of orientation to time or place

- Any occurrences of unsafe driving behavior
- Suspicion of dementia should lead to a full evaluation

Slide 25:

- Persons living with dementia typically have memory impairments and, thus, may forget they have memory problems. They may also lack insight into, awareness of, and understanding about their impairments. Some persons with dementia may give incomplete or unreliable information because they are in denial of their impairments.
- Consequently, it is very important to get supportive documentation from a knowledgeable informant such as a spouse, family member, close friend, or other care partner. Preferably, the conversation with the informant should be conducted without the persons living with dementia in the room to allow for a more open conversation. Ideally, it is done after the interview with the persons living with dementia.
- Within the policies associated with the Health Insurance Portability and Accountability Act (HIPAA), clinicians can ask the informant to note whether the person has any of the warning signs of dementia—not just memory impairments, but impairments that interfere with daily functioning. For example, does the person repeat questions or stories? Lose or misplace objects? Has there been any change to mood or behavior or gait? Any inappropriate behaviors or disinhibition? Are there other symptoms that are of concern?
- Some screening tools are specifically geared toward informants such as the Short Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), the Ascertain Dementia 8-item Informant Questionnaire (AD8), which can be administered in-person or by phone, or the General Practitioner Assessment of Cognition (GPCOG) informant component. Although the IQCODE is one of the most commonly used tools, only one study has tested its diagnostic accuracy.
- However, it should be noted that not all persons living with dementia have an identified informant.

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- Many cognitive tests are available, but not all are appropriate for use with all persons.
- Cognitive screening tests suitable for short primary care visits are 5 or fewer minutes to administer and have been validated in a primary care or community setting.
- The test must be easy to administer by medical staff members who are not physicians and should be relatively free of educational, language, and/or culture biases. It should also have good-to-excellent psychometric properties, and should be validated in the primary care setting. Finally, clinical staff should be able to use it without copyright fees.

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- Commonly used brief assessment tools include:
 - Ascertain Dementia (AD8)
 - Mental Status Questionnaire (MSQ)
 - Mini-Cognitive Assessment Instrument (Mini-Cog)
 - Rapid Cognitive Screen (RGS)

- Short Blessed Test (SBT)
- Short Test of Mental Status (STMS)
- Short Portable Mental Status Questionnaire (SPMSQ)
- Six Item Screener (SIS)

Slide 29:

- Not all meet suitable criteria as defined by the AWW recommendations.
- The Mini-Cog is shorter and less-culture-bound than the MMSE (see below). It involves drawing a clock, in which a person is asked to draw a clock indicating a specific time, along with a three-item memory test. It tests visuospatial, executive function, planning, and memory function. However, there have not been sufficient studies on the Mini-Cog to determine its accuracy in diagnosing Alzheimer's disease and other dementias; as such it should be used as a screening tool (Fage, Chan, Gill, Noel-Storr, Hermann, Smailagic, ... & Seitz, 2015).
- The MMSE has some important limitations associated with its routine use. In addition to being copyrighted and proprietary (it is no longer in the public domain and free), it takes between 5 and 10 minutes to administer and has a high rate of false positives, especially with persons of lower education, and false negatives among highly educated persons with cognitive impairments. It is most appropriate for persons with at least moderate cognitive impairment. It is not sufficiently effective in detecting early dementia, but it can be used to grade established dementia (Cooper & Greene, 2005). A 2015 Cochrane review did not find evidence supporting a substantial role of the MMSE when used alone to identify persons with mild cognitive impairment who could develop dementia (Arevalo-Rodriguez et al., 2015). The most recent Cochrane review on the MMSE indicates that **it can be a part of the process for deciding whether a person has dementia, but the results will need to be interpreted within a broader context of additional signs and symptoms** (Creavin et al., 2016). An alternative option is the Addenbrooke's Cognitive Examination (or ACE), which addresses some of the deficiencies of the MMSE (Cooper & Greene 2005; Dudas, Berrios, & Hodges, 2005). The American Academy of Family Physicians (AAFP) has a searchable database of cognitive evaluation tools.

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- In addition to a structured cognitive assessment, a full evaluation for a person who is suspected of having dementia can involve additional neurocognitive testing by a neurologist, neuropsychologist, or neuropsychiatrist, along with laboratory tests and imaging studies ordered by the primary care provider, neurologist, or neuropsychiatrist to rule out secondary causes of dementia.
- In some cases, evaluation will be based on information from the care partner. For example, the care partner of a person suspected of dementia might be administered the screening component of the Neuropsychiatric Inventory (or NPI) on behalf of the person being screened for dementia, and would be asked to complete the entire inventory in the event of a positive screen. However, while the NPI has been shown to be able to distinguish between people with and those without dementia, it is less able to distinguish between the different types of dementia.
- Typically, the neurologic system is normal, as is a physical examination, although the latter may provide evidence about the possible type of dementia if there are focal deficits from a prior

stroke, suggestive of vascular dementia, or Parkinsonian symptoms, suggestive of Lewy body dementias.

- Persons with an atypical presentation, such as those with an early age of onset, sudden onset, or who lack sufficient objective evidence of progressive cognitive decline, require additional evaluation by a specialist.

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- A wide range of medical and psychiatric illnesses can be included in a differential diagnosis. Consequently, persons suspected of having dementia may need lab work to rule out some of these options. Typically, the lab work includes a comprehensive metabolic profile, complete blood count, thyroid stimulating hormone, and a test for levels of vitamin B12. If appropriate, the rapid plasma reagin (RPR) test for syphilis, a urinalysis, and testing for HIV may be requested. The American Geriatrics Society also recommends including tests for folate levels and calcium levels. Some persons may require a toxicology screen or a test for heavy metal.
- Neuroimaging is typically not included in the initial workup unless the person has early onset dementia, an abrupt onset with rapid cognitive decline, focal neurologic symptoms, or predisposing conditions such as HIV disease or a malignancy or there is suspicion of a subdural hematoma, normal pressure hydrocephalus, or infection. Often, computerized tomography (or CT) scans are sufficient, although persons suspected of vascular dementia may require magnetic resonance imaging (or MRI).
- Genetic tests are rarely required for most persons suspected of having dementia. However, they may be of benefit for persons suspected of having early or very early onset dementia, frontotemporal degeneration (or FTD), or other familial dementias.

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- There is a large and evolving body of evidence supporting the use of biomarkers in diagnosing dementia.
- Biomarkers of brain amyloid-beta (or A β) protein depositions include low cerebrospinal fluid (CSF) A β 42 and positive positron emission tomography (or PET) amyloid imaging.
 - CSF is used routinely in Europe and for many patients in the United States
 - There are currently 3 tracers with FDA approval for brain amyloid PET imaging: florbetapir, flutemetamol, and florbetaben. They are not covered by Medicare but are available to the general public.
- A recent meta-review found that combining the two biomarkers affords the highest sensitivity and specificity; can differentiate between Alzheimer's disease and normal/healthy controls; and can predict which persons living with mild cognitive impairment will progress to dementia.
- However, no CSF core biomarkers are effective in consistently distinguishing between Alzheimer's disease and other forms of dementia.

Slide 34:

- A wide range of treatable conditions can cause cognitive impairment and should therefore be included in a differential diagnosis.

- The so-called 3D's of geriatric psychiatry include dementia, delirium, and depression. They have many similar symptoms, but their treatment and prognosis are very different. It is important to correctly identify a diagnosis. We will cover delirium and depression in more depth, next.
- Other possible treatable causes of cognitive impairment include a deficiency of vitamin B12, thiamine, or folate; specific endocrine disorders such as thyroid or parathyroid problems; and normal pressure hydrocephalus (or NPH).
- Infections (from urinary tract infection to meningitis or syphilis) can also lead to cognitive impairment.
- Similarly, specific diseases (such as systemic lupus erythematosus, sarcoidosis, chronic obstructive pulmonary disorder, congestive heart failure, and liver disease) may include cognitive impairment as a manifestation.
- Alcoholism, medication overdose or misuse, and drug toxicity can all cause or manifest as cognitive impairment.
- Sleep disorders, including obstructive sleep apnea, may also cause cognitive impairments.
- Finally, brain tumors or lesions can manifest with many symptoms of dementia, including cognitive impairment.

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- Delirium is an acute, temporary state of mental confusion with an abrupt onset.
- It can occur anywhere and at any time—when the person is at home, in an acute-care hospital, or in a long-term facility. However, nearly 30 percent of older patients experience delirium at some time during hospitalization; the incidence is higher in intensive care units.
- It is characterized by altered consciousness, impaired attention, and disorganized or delusional thinking. The person with delirium has difficulty focusing and paying attention. He or she may have hallucinations and delusions, especially visual. The symptoms typically worsen at night.
- It is important to accurately recognize and diagnose delirium, because it is independently associated with increased all-cause morbidity and mortality.
- There are different types of delirium—one that manifests with hyperactivity (such as agitation, restlessness, irritability, or hallucinations) and one that manifests with hypoactivity (such as somnolence, decreased motor activities, or diminished vocalizations). There is also a mixed form, in which the person has symptoms of both hyper- and hypo-activity.
- Delirium is a risk factor for dementia and can worsen underlying dementia, particularly in very old persons. The interprofessional team should educate care partners about delirium and instruct them to alert the primary care provider immediately if any persons living with dementia exhibits symptoms of delirium.
- The Confusion Assessment Method (CAM) is typically used to help diagnose and monitor delirium. Suspicion of delirium should be raised if there is both an acute onset and a fluctuating course of symptoms, along with the other symptoms.

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- Depression is considered the third “D” of geriatric psychiatry (dementia, delirium, and depression). Depression is not a normal consequence of aging.

- Older persons often have atypical nonspecific presentations of depression; however, if it is not identified early, minor depressive symptoms can progress to major depression (Ellison, Kyomen & Harper, 2012).
- Symptoms of depression in the older patient include somatic complaints of pain, unintentional change in weight/appetite, chronic constipation, irritability, agitation, fatigue, headache, insomnia, motor retardation, hypersomnia or other sleep disturbances, and weakness (Ellison, et al., 2012; Cooper & Greene, 2005; Downing, Caprio & Lyness, 2013).
- Depression can impair cognition, with or without delirium or dementia.
- Both delirium and dementia are associated with a higher rate of depression (Downing et al., 2013). It is estimated that more than 10 percent of older adults in primary care practices have depression (Lyness, Yu, Tang, Tu, & Conwell, 2009).
- The three most commonly used validated tools to screen for depression in the geriatric patient are the Geriatric Depression Scale (or GDS), the 9-item Patient Health Questionnaire (or PHQ-9), and the Cornell Scale for Depression in Dementia (Phillips, 2012). Once diagnosed, older persons with depression may require counseling and/or pharmacotherapy.

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- This table compares dementia, delirium, and depression. They are not mutually exclusive, and a person can have all three at the same time.
- However, as you can see, specific factors can help a clinician distinguish among the 3D's. For example, depressive symptoms do not fluctuate throughout the day, nor do they include disorientation. However, both dementia and depression may manifest with somatic complaints.

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- Looking at the outline, we now move from recognizing and diagnosing dementia to focusing on the specific type of dementia the person is living with, with particular emphasis on Alzheimer's disease and related dementias—including vascular dementia, Lewy body dementias, and frontotemporal degeneration. We also will look at the diagnosis of early onset dementia.

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- The original criteria for diagnosing Alzheimer's disease were developed by the National Institute on Neurological and Communicative Disorders and Stroke (or NINCDS) and the Alzheimer's Disease and Related Disorders Association (or ADRDA) workgroup in 1984.
- These criteria were updated and significantly revised in 2011 by the National Institute on Aging in conjunction with the Alzheimer's Association based on increased understanding of the disease. These new consensus criteria incorporate two substantial changes. First, there is recognition of three stages of Alzheimer's disease, progressing from a preclinical stage that occurs before any changes in cognition or functional impairments can be detected; through a stage of mild cognitive impairment due to Alzheimer's disease, which is characterized by the emergence of cognitive symptoms that are not sufficient to meet criteria for a diagnosis of Alzheimer's disease; and, in many persons to Alzheimer's disease dementia, in which day-to-day function is impaired. The second major change concerns the incorporation of biomarkers.

- The research leading to the new diagnostic criteria distinguishes between Alzheimer's disease and Alzheimer's disease dementia. However, throughout these modules, we are using the term "Alzheimer's disease" to mean dementia caused by Alzheimer's disease.
- Specifically, the recent guidelines recognize that the pathophysiologic process underlying Alzheimer's disease begins years (and possibly decades) before there are detectable cognitive changes and onset of clinical dementia (Jack et al., 2011; Sperling et al., 2011). Investigators note that not all persons with evidence of early Alzheimer's disease pathology will eventually progress to clinical Alzheimer's disease dementia (as they called it) (Jack et al., 2011; Sperling et al., 2011).
- The new diagnostic criteria also reflect the growing understanding of the genetics of Alzheimer's disease and recognize biomarkers of brain amyloid beta protein deposition, including low cerebrospinal fluid AB42 and positive PET amyloid imaging. (Jack et al., 2011).

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- Although mild cognitive impairment is considered by most to be a precursor to dementia, there are cases when MCI resolves and the person returns to normal. In addition, persons living with MCI, by definition, have cognitive impairments that are not normal for their age but fail to meet the criteria for dementia.
 - Persons with MCI are not demented, but they may demonstrate objective evidence of (typically mild) cognitive impairment in a cognitive assessment—but without interference with functional abilities.
- MCI should be assessed by the primary care professional over time to monitor progression or regression.
- It is important to evaluate the person living with MCI for the presence of other brain diseases or systemic causes that could be causing the impairments. Biomarkers can increase certainty of MCI but are not routinely recommended.

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- Although amyloid beta (or Ab) protein plaques are one of the defining pathological features of Alzheimer's disease, they are found in many otherwise normal older persons, as well as in persons with clinical syndromes other than Alzheimer's disease.
- The Amyloid Imaging Task Force (or AIT), developed and convened by the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in conjunction with the Alzheimer's Association, developed recommendations to identify appropriate use criteria for PET amyloid imaging.
- According to the AIT appropriate use criteria, Amyloid PET imaging can be used in an individual with MCI or dementia (1) in whom the cause of the cognitive impairment is uncertain after a standard examination by an experienced clinician, and (2) for whom it is determined that knowledge of amyloid status will change the person's diagnosis and management (Rabinovici et al., 2016). It is therefore appropriate for persons with an atypical presentation or a relatively young age at onset (<65 years). Amyloid imaging is inappropriate in the following situations:
 - Persons who meet standard criteria for MCI or AD with typical age of onset.
 - Persons who are asymptomatic or who have a cognitive complaint that is unconfirmed on clinical examination.

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- The criteria for diagnosing vascular dementia (or VaD) are not as clear-cut as those for some of the other forms of dementia.
- It can be difficult to provide a differential diagnosis of vascular dementia versus Alzheimer's disease without knowledge or evidence of a history of stroke or other disorders of the heart and blood vessels.
- A wide range of diseases and conditions have been linked with vascular dementia and cognitive impairment:
 - Atherosclerosis, hyperlipidemia, and atrial fibrillation (De Bruijn, Heeringa, Wolters, Franco, Stricker, Hofman, & Ikram, 2015)
 - Diabetes mellitus, hyperglycemia, insulin resistance, and metabolic syndrome (Biessels, Strachan, Visseren, Kappelle, & Whitmer, 2015)
 - Cerebrovascular disease, small vessel disease, systemic lupus erythematosus, temporal arteritis, and brain hemorrhage as well as chronic kidney disease and amyloid angiopathy
- Prior stroke or heart attack with an increased risk of Alzheimer's disease and vascular cognitive impairment (Sahathevan, Brodtmann, & Donnan, 2011)
- The procedure for making a diagnosis of vascular dementia is similar to that associated with a diagnosis of Alzheimer's disease, although it is important to identify underlying cardiovascular or cerebrovascular diseases, among other conditions.
- For persons meeting the criteria for dementia, evaluation of blood pressure, cholesterol, and blood sugar may provide clues of a vascular dementia. Persons likely need a referral to a neurology specialist for a neurological exam and neuroimaging to identify a history of transient ischemic attacks, strokes, blood vessel changes, or tumors. A differential diagnosis would include thyroid disorders and vitamin deficiencies.

Slide 45:

- Lewy body dementia (or LBD) syndromes encompass dementia with Lewy bodies (or DLB) and Parkinson's disease dementia (or PDD).
- A major distinction between DLB and PDD is the temporal sequence of appearance of clinical symptoms (Mrak & Griffin, 2007):
 - Specifically, DLB is diagnosed when dementia onset occurs <1 year after Parkinsonian symptoms appear, whereas PDD is diagnosed if the onset of dementia occurs several years after Parkinsonian symptoms appear or Parkinson's disease has been diagnosed (McKeith et al., 2005; Mrak & Griffin, 2007).
 - However, it can be difficult to apply the "1-year rule" distinguishing between the two disorders in clinical practice (McKeith et al., 2005).

Slide 46:

- There are similarities and differences to help distinguish between LBD and Alzheimer's disease:
 - Memory impairment is not a prominent early feature of LBD, in contrast to Alzheimer's disease, although it does commonly manifest later in the disease process.

- The clinical manifestations of LBD and late-stage Alzheimer's disease become more similar over time.
- Evidence suggests that the mean age of onset of DLB is similar to that of Alzheimer's disease, around age 68, whereas Parkinson's disease has an earlier age of onset of 60 years. However, there appears to be a more rapid course from onset or diagnosis of DLB to institutionalization compared with Alzheimer's disease or other dementias.

Slide 47:

- The symptoms of frontotemporal degeneration, which is also known as frontotemporal disorder, frontotemporal dementia, or frontotemporal lobar degeneration are sufficiently different from Alzheimer's disease to enable a quicker differential diagnosis between the two types of dementia.
- The person with FTD is generally younger at onset, has a rapid progression of dementia, and has more psychiatric symptomatology than the person with Alzheimer's disease.
- Persons with FTD have relatively preserved memory and visuospatial abilities compared with persons with Alzheimer's disease. There is likely to be greater apathy, disinhibition, and impulsivity in the person with behavioral variety FTD (or bvFTD) than in the person with Alzheimer's disease, and the person with FTD frequently lacks insight into their disease and its consequences (Cardarelli, Kertesz, & Knebl, 2010).
- While imaging studies may document atrophy of frontal or temporal lobes, this finding is also common among persons with LBD or Alzheimer's disease.

Slide 48:

- Symptomatic presentation of language-related FTD also differs from that of Alzheimer's disease. Persons with semantic variant FTD (or sFTD) and primary progressive aphasia (or PPA) have clear language impairments:
 - Persons with sFTD have effortless but meaningless speech; they use broad generic terms instead of specific terms (animal vs. dog, food vs. cereal). They may not be able to recognize familiar faces, such as those of well-known celebrities. The person with sFTD may also demonstrate behavioral manifestations similar to those with bvFTD.
- Persons with progressive nonfluent aphasia (or PNA) have nonfluent, hesitant speech that requires substantial effort. They have difficulties finding the right word or naming objects. They may also have impaired comprehension with a limited speech output. During early-stage PNA, persons have preserved social and behavioral skills, but this deteriorates with disease progression (Cardarelli et al 2010).
- Up to 50 percent of persons living with bvFTD have been misdiagnosed as having either major depression or another psychiatric disorder, particularly late onset bipolar disorder, late onset schizophrenia-like psychosis, late onset depression, or late onset.
- International consensus criteria were recently revised for the diagnosis of behavioral variant frontotemporal disorder.

Slide 49

- As was mentioned in Module 1, persons are considered to have early onset dementia (or EOD) if they are diagnosed before the age of 65.

- There is an extensive list of conditions to consider in a differential diagnosis of EOD, including early onset forms of neurodegenerative disorders, late onset forms of childhood neurodegenerative conditions, and potentially reversible etiologies. The diagnosis is frequently delayed, even more so than that with late onset dementia because early onset is considered rare and is often overlooked at the primary care level.
- When making a differential diagnosis between EOD and psychiatric disorders, it is important to remember that the signs and symptoms suggestive of psychiatric illness include an abrupt onset, identifiable emotional precipitating factor, and lack of progression over time.
- A diagnosis of EOD requires a thorough clinical assessment including patient history (with informant corroboration), behavioral features and psychiatric history, degree of functional impairment, temporal profile of the mode of onset and the progression of symptoms, medical history, social history (including educational and occupational attainment), and family history of neuropsychiatric illnesses.
- Other important points may include specific dementia risk factors such as head injury with loss of consciousness or alcohol/drug exposure. Formal cognitive evaluations can identify the affected cognitive domains.
- A “dementia-plus” algorithm has been proposed as a framework for the clinical assessment and diagnosis of EOD.
 - Combining patient history, clinical manifestations, and neurological findings can help lead to consideration of EOD: Laboratory investigations may help rule out toxic/metabolic encephalopathies, infectious etiologies, or autoimmune illnesses.
 - Persons suspected of living with EOD are often recommended to undergo neuroimaging, particularly MRI, along with CSF analysis.

Slide 50:

- The items below are provided to allow faculty to evaluate what students have learned. The items can be used in several ways including given at the end of the lecture to assess knowledge or as an evaluation to assess knowledge gain. These items have face validity. Psychometric testing was not conducted on these items.

Answers

1. b. Provides an opportunity for the person to make treatment decisions while he/she retains adequate cognitive functioning
2. a. Universal screening for cognitive impairment using formal instruments

Slide 51:

Answers

3. b. Dementia with Lewy bodies
4. c. Mini-Cog