Approach to the Older Adult With New Cognitive Symptoms

Ericka E. Tung, MD, MPH; Victoria Walston, MD; and Mairead Bartley, MB, BCh, BAO, MD

Abstract

Dementia affects nearly 50 million people worldwide, translating into one new case every 3 seconds. Dementia syndrome is one of the leading causes of disability among older adults, yet it remains vastly underdiagnosed. A timely diagnosis of dementia is essential to ensuring optimal care and support of individuals and their loved ones. Although there is no single test for dementia, health care providers can use a structured approach to the workup and management of new cognitive symptoms. Comprehensive MEDLINE and PubMed searches were performed to develop an unbiased, practical diagnostic approach to these symptoms. This review guides primary care providers in the workup, diagnosis, delivery, and initial management of patients presenting with new cognitive symptoms.

Dementia represents one of the largest global public health challenges facing modern society. Data from the World Health Organization suggests that 50 million individuals worldwide struggle with dementia; this number is expected to triple in the next 30 years. Dementia is the most common cause of disability among older adults due to affected individuals’ gradual loss of independence and progressive increase in neuropsychologic symptoms. This syndrome poses an enormous emotional and financial burden on family care partners who provide more than $200 billion in uncompensated care annually. As a comorbidity, dementia increases the costs of delivering care by nearly 50% when it coexists with other chronic conditions such as diabetes and coronary artery disease.

The impact of dementia on patients, their loved ones, and their communities is far reaching, making it critical for all health care teams to recognize the signs and symptoms of early dementia and to develop effective diagnostic and management skills. Despite this clinical imperative, delays in the diagnosis of dementia remain common, with most individuals suffering with symptoms for an average of 3 to 5 years before the diagnosis is made. Fewer than 50% of individuals ever receive a formal diagnosis, placing an enormous emotional toll of anxiety on both individuals with dementia and their families. Most importantly, without a diagnosis, education, or action planning, older adults with cognitive impairment are at high risk for crisis-driven management such as acute hospitalizations, critical care unit admissions, and premature institutionalization.

This clinical review aims to provide frontline clinicians with a practical, evidence-based approach to managing the patient with new cognitive symptoms in the ambulatory care setting. For this review, we conducted a comprehensive and systematic search of Ovid MEDLINE and Ovid PsycINFO, PubMed from 1946 to April 15, 2019, including the terms cognitive disorders, cognitive dysfunction, dementia, primary health care, diagnosis, geriatric assessment, and neurocognitive tests to develop an unbiased focus on the diagnostic approach to cognitive impairment.

DIAGNOSTIC CRITERIA AND DEFINITIONS

Published in 2013, the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) offered several substantive changes over the DSM-4. Specifically,
dementia was renamed major neurocognitive disorder (major NCD) and the term mild neurocognitive disorder (mild NCD, also called mild cognitive impairment [MCI]) was added to acknowledge earlier manifestations of cognitive change. Respective terms are equivalent and can be used interchangeably. The purpose of this change in nomenclature was two-fold: to reduce social stigma and to encapsulate the myriad of etiologies and manifestations of cognitive impairment. This version also described two new cognitive domains that can be affected by dementia: complex attention and social cognition. Cognitive domains detailed in the DSM-5 are listed in Table 1.

The diagnosis of dementia (major NCD) requires one to have a decline from a previous level of functioning in one or more cognitive domains which interferes with daily function and independence. Memory impairment is no longer a required criterion. The progressive decline must not be due to delirium or other mental health conditions. MCI (also known as mild NCD) is an intermediate clinical state characterized by an objective decrease in cognitive functioning that does not interfere with one’s ability to participate in complex activities, although greater effort or time may be required.

The National Institute on Aging and Alzheimer’s Association (NIA-AA) developed separate diagnostic recommendations to allow for clinical decision making and to provide a common diagnostic lexicon for future Alzheimer disease research. This 2011 guideline described three phases of Alzheimer disease (AD): preclinical AD, mild cognitive or prodromal AD, and dementia caused by AD. These phases are further classified based upon biomarkers found in the cerebrospinal (CSF) fluid, such as β-amyloid and pathologic tau, shifting the definition of AD to a biological construct. Whereas these biomarkers are not yet a recommended part of the initial workup of uncomplicated cognitive impairment, the NIA-AA guidelines form the foundation of future neurocognitive research on the diagnosis of dementia.10

**SUBTYPES**

AD remains the most common of the neurodegenerative conditions causing dementia, comprising 70% to 80% of dementia cases. However, given the prevalence of dementia with Lewy bodies, vascular dementia, and frontotemporal dementias, these subtypes are also common to the primary care practice. Mixed dementia with features of multiple subtypes is also common. Distinctive clinical features have been described with each of these syndromes (Table 2).

**RISK FACTORS**

Given the heterogeneity of dementia, risk factors vary for different subtypes of the syndrome and can be categorized as nonmodifiable and modifiable. Age is the most important nonmodifiable risk factor for developing any subtype of dementia. Genetic risk factors have been well studied in AD. Having one parent with dementia doubles one’s risk; however, this risk declines with advancing parental age at the time of diagnosis.18 Early-onset AD is rare and typically follows an autosomal dominant inheritance

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**TABLE 1. DSM-5 Cognitive Domains**

<table>
<thead>
<tr>
<th>Cognitive domain</th>
<th>Capacities</th>
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<tr>
<td>Complex attention</td>
<td>Selective attention, processing speed</td>
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<tr>
<td>Executive function</td>
<td>Planning, organization, decision making</td>
</tr>
<tr>
<td>Learning and memory</td>
<td>Encoding new information, free and cued recall</td>
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<tr>
<td>Language</td>
<td>Word finding, naming, grammar, and syntax</td>
</tr>
<tr>
<td>Perceptual-motor function</td>
<td>Visual perception, visuococonstructional reasoning, perceptual-motor coordination</td>
</tr>
<tr>
<td>Social cognition</td>
<td>Awareness of one’s own emotions and insight of other’s perception of oneself</td>
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*DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.
Derived from the American Psychiatric Association.*
Late-onset AD is influenced by a more complicated set of genetic factors, with apolipoprotein E epsilon 4 being the most firmly established genetic risk factor.

Modifiable risk factors can be categorized into those impacting individuals in early life (age <18 years), midlife (age 45 to 64 years), and later life (age >65 years) based on estimates of the population attributable fraction. The most notable early-life risk factor is lower educational attainment, defined as no secondary school education.19 Midlife risk factors include uncontrolled hypertension, smoking, severe brain injury, and obesity. Hearing loss has also been recently identified as a highly prevalent modifiable risk factor.20,21 Later-life risk factors such as smoking, depression, sedentary lifestyle,22 social isolation, and diabetes are associated with increased risk of developing multiple subtypes of dementia.19

**SCREENING VERSUS A TIMELY DIAGNOSIS**

The most recent recommendation from the US Preventive Services Taskforces (USPSTF) states that current data are insufficient to assess the balance of benefits and harms of routine screening for dementia. USPSTF provides additional clarification around this statement, stating that this screening recommendation is focused on those adults aged 65 years and older who do not have any signs or symptoms of cognitive impairment.23 Conversely, prompt recognition of new cognitive symptoms that interfere with social, occupational, or other daily life functions and resultant workup comprises a “timely diagnosis.”24

A timely diagnosis allows patients and care partners to work closely with their health care teams to build upon existing capacities, anticipate future challenges, and assemble care partnering and caregiving systems. Early recognition also allows for the development of safe, patient-centered care plans that aim to prevent crisis-driven management decisions in the acute care setting. To achieve this, clinicians must be attuned to the early symptoms and signs of dementia.

<table>
<thead>
<tr>
<th>TABLE 2. Dementia Subtypes</th>
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<tr>
<td>Subtype</td>
</tr>
<tr>
<td>AD</td>
</tr>
<tr>
<td>With Lewy bodies</td>
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<tr>
<td>Vestibular</td>
</tr>
<tr>
<td>PD</td>
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<tr>
<td>Frontotemporal variant</td>
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AD = Alzheimer disease; CT = computed tomography; MRI = magnetic resonance imaging; PD = Parkinson disease; REM = rapid eye movement.
Clinical changes may be first recognized by the patient, spouse, or other informant. These changes may occur in one or more domains including retention of new information, ability to manage complex tasks, ability to cope with unexpected events, difficulty with word finding, changes in personal or social behavior, or challenges in spatial ability.

MAKING THE DIAGNOSIS

Clinical History
The goals of any evaluation should be to first acknowledge the patient/caregiver concerns, objectively identify cognitive decline, document functional status, and discern whether an underlying neurodegenerative disorder or other medical or psychiatric cause is present. Clinical concern of a change in cognitive function is important to describe, in line with diagnostic criteria described earlier. In particular, it is important to clarify whether cognitive concern is associated with functional implications. Important information can be gathered from the moment the patient arrives for the visit. For example, patients missing or arriving late for appointments, arriving unkempt, or having no or little knowledge of medications may indicate a problem. As function becomes impaired due to cognitive decline, the ensuing safety consequences, both for the person themselves and also for the general public, must be discussed. Is the patient cooking on an open flame? Is the patient a driver? Are they still able to manage their own medications? Typically, basic activities of daily living are maintained until later in the course; however, instrumental activities, such as financial management, may be affected early on. The Functional Activities Questionnaire is one questionnaire which can be used to assess Instrumental Activities of Daily Living function and can later be used to track progression.25,26

Physical Examination
Performing a mental status examination forms the core of the examination of a patient presenting with cognitive concerns. Components of the mental status examination include appearance, behavior, motor activity, mood/affect, thought process/content, perception, insight, cognition, and judgement.27

The physical examination should be comprehensive, with special focus on the neurologic examination which may help characterize the etiology of cognitive impairment (Table 2). For example, one may be able to identify clinical features of parkinsonism, gait impairment, frontal signs, or evidence of prior stroke. Cardiovascular examination should be tailored to vascular risks and also look for orthostatic hypotension. Other areas of focus on clinical examination may depend on concerns raised from the clinical history; for example, a history of unintentional significant weight loss in the context of cognitive decline would warrant a review for underlying malignancy.

Cognitive Testing
There is a myriad of cognitive tests available. With the introduction of the annual wellness visit in 2011 and its recommendation to assess cognition, the Alzheimer’s Association convened a workgroup to develop recommendations to help guide primary care providers.28 Within this, they recommended an initial structured assessment to serve as a baseline or to trigger further evaluation. To provide clarity for providers in selecting an initial cognitive assessment screening tool, the workgroup sought to identify tools that would be quick to administer, validated in primary care, easy to administer by nonclinical staff, and free of charge and bias. An example of one such tool is the Mini-Cog,29 which tests 3-item recall and a clock draw test. When choosing a cognitive assessment tool, providers should ensure it has been validated in the population being seen. For example, the Mini-Cog has been validated in many different populations.29-31 The Alzheimer’s Association workgroup does note that other tools can be used at the “discretion of the clinician.” As noted, these initial brief tests help to risk stratify, not to follow the patient longitudinally, and if abnormal, indicate the need for further.
mental status testing. The USPTF examined instruments which could be administered by a provider in less than 10 minutes or be self-administered in 20 minutes. The Mini Mental State Examination (MMSE) was the most commonly studied. However, this is now a proprietary test, which has limited its widespread use. Also, it is less effective at distinguishing cognitively healthy from people with MCI and is influenced by age and education.

The Montreal Cognitive Assessment is another commonly used and validated test, which also has the advantage of being available in several languages other than English. It takes approximately 10 minutes to administer and is a 30-point test which assesses domains of visuospatial/executive function, naming, attention, language, memory, delayed recall, orientation, and abstraction. Normal score range is 26 or greater with allowance made for educational status of the patient. Health care providers are required to be trained and certified to use the Montreal Cognitive Assessment through the online standardized training and certification test. An alternative option is the Short Test of Mental Status, a 38-point cognitive test that has been validated in dementia cohorts and tests orientation, attention, immediate recall, arithmetic, abstraction, construction, information, and delayed recall. A score of 29 or less is suggestive of underlying dementia.

Whatever test is used, the results should be considered, along with the history and examination, to help guide the need for further testing. In some situations, referral for formal neuropsychologic testing is indicated to further characterize the cognitive deficits and confirm the diagnosis, for example, in younger patients, atypical presentations, cases of rapid cognitive decline, or where there is a question of current functional capacity. Formal neuropsychologic testing can add helpful insight into the etiology of the diagnosis and help determine functional limitations. The American Academy of Neurology practice guideline update on MCI recommends further assessment such as with neuropsychologic testing for those who have scores indicating MCI on brief cognitive tests because brief cognitive tests are usually more sensitive than specific. They also recommend referral to a specialist if the provider is inexperienced in dealing with patients with cognitive impairment. Formal neuropsychologic testing takes several hours to complete. Hence, consideration for the patient’s ability to participate in this testing, particularly taking into account the stage of cognitive impairment at which they may have presented to primary care, other comorbidities, their goals of care, and certainty of diagnosis may influence the decision to refer for neuropsychologic testing.

Differential Diagnosis
In the evaluation of a patient with new cognitive symptoms, the clinician must be attuned to the possibility of other non-dementia conditions that can also present with cognitive symptoms. A thorough history, establishment of time course, and physical examination are critical first steps in this evaluation.

Identification of depression is an important consideration in older adults with cognitive symptoms, as it is well established that depression is highly prevalent among older adults, and is associated with poorer cognition and quality of life. Depression has been recognized as both a risk factor and a prodromal syndrome for dementia. Several factors challenge one’s ability to make the diagnosis of depression in dementia including older adults’ tendency to present with atypical mood symptoms, limited ability to convey emotional symptoms, and the fact that standard assessment tools often require the patient to recall recent symptom burden. Tools such as the Cornell Scale for Depression in Dementia and the Hamilton Depression Rating Scale offer higher sensitivity for detection of depression in dementia as both require input from a care partner or collateral historian.

Although no clear time frame has been defined, in patients for whom first symptom onset to development of dementia encompasses less than a year (oftentimes on the order of weeks to months), attention to causes
of rapidly progressive dementia and an ensuing wide differential should be considered. It is important to exclude delirium as an alternative diagnosis in patients who present with rapid onset of cognitive impairment.45 One commonly used mnemonic for the differential of rapidly progressive cognitive symptoms is the acronym VITAMINS. This stands for vascular, infectious, toxic-metabolic, autoimmune, metastases/neoplasm-related, iatrogenic, neurodegenerative, and systemic/seizures/structural etiologies that should be considered when symptoms are rapidly progressive.46

Laboratory Studies
Standard laboratory evaluation of the patient with new cognitive impairment is directed toward identifying medical illness that can cause or contribute to these symptoms. Current consensus in the literature and guidelines support initially obtaining thyroid function tests and a vitamin B12 level.47 Based on individual considerations, overnight oximetry, complete blood count, electrolyte panel, HIV, and syphilis testing may also be warranted.

In patients younger than 55 years with cognitive impairment, those with a rapidly progressive disease course, atypical dementia syndromes, or those who are immunosuppressed, CSF examination is warranted to exclude infection, malignancy, and neuroinflammation.50 Routinely obtaining CSF biomarkers, such as tau and amyloid beta 1-42 in AD51—53 in the primary care evaluation of patients with cognitive impairment is currently not recommended for diagnostic purposes.48 However, this remains an area of active research and, in the correct clinical context, CSF biomarkers may provide insight into the underlying cause. Although specific biomarkers differ among the dementia syndromes, their potential to allow preclinical diagnosis, monitor disease progression, and indicate underlying pathology remains promising.44—45

Imaging Studies
Structural imaging of the brain (computed tomography [CT] or magnetic resonance imaging [MRI]) is recommended by most national guidelines when evaluating patients for dementia. It is important to rule out secondary causes of cognitive impairment such as tumor, normal pressure hydrocephalus, stroke, and associated vascular disease, demyelination, or chronic infection.47,48,58

MRI is generally preferred over CT due to greater sensitivity for various pathologies and lack of exposure to ionizing radiation. However, CT remains a reasonable option if a patient is unable to tolerate MRI or in the acute setting evaluation when hemorrhage or stroke must be ruled out quickly. Noncontrast imaging is usually adequate for routine evaluation of patients with suspected cognitive impairment, whereas intravenous contrast should be considered when there is a concern for CNS infection, neoplasm, or in patients with unexplained neurologic deficits.

Although imaging findings vary across dementia syndromes (Table 2), cerebral atrophy to a greater extent of that seen in normal aging is characteristic of neurodegenerative dementia. Patterns and degree of brain atrophy correlate with positive predictive values for different dementia syndromes and are incorporated into diagnostic criteria.58 In AD, brain atrophy correlates with both tau deposition as well as neuropsychologic deficits and at the cognitive impairment stage, the degree of medial temporal structure atrophy, including the hippocampus, are suggestive of AD.59 Functional brain imaging is an area of ongoing evolution. Modalities of 18-F-fluorodeoxyglucose positron-emission tomography and single-photon emission computed tomography using specific tracers reveal areas of brain hypometabolism and hypoperfusion, respectively, which can be seen in distinctive patterns among dementia syndromes. Several positron-emission tomography tracers that bind to and label specific proteins (fibrillar amyloid and tau) allow for in vivo evaluation of the molecular pathology underlying dementia subtypes (such as AD).54 Although an area of active research, these modalities currently have limited clinical utility in primary care evaluation as the imaging
techniques are costly and require substantial expertise to perform and interpret.

**Dementia Subtype**
Based on the clinical history, mental status examination, physical examination, and laboratory and imaging studies, the clinician can postulate the subtype of dementia. Key clinical and imaging features of common dementia subtypes are listed in Table 2. Understanding the subtype of dementia can inform treatment decisions, prognosis, and anticipatory guidance. With the future advancement of functional imaging and biologic markers of dementia, clinicians will be able to determine the dementia subtype with more certainty.

**DELIVERING THE DIAGNOSIS**
Although awareness of dementia is increasing, we know that historic rates of diagnosis are low, particularly in primary care.60,61 Barriers to making a timely diagnosis include time constraints in a limited office visit where there may be many other things to address, perceived futility of making a diagnosis with little treatment options available, under-recognition of a problem by family,62,63,64 and lack of prior provider experience in dealing with dementia.63,64 One strategy which may be helpful when cognitive concerns are raised is to schedule a family meeting or dedicated visit with a collateral historian present.26

At the dedicated visit, the clinician should communicate the diagnosis to the patient and family in a clear, compassionate, and straightforward manner. At this visit, the clinician can assess how much information the patient and family are ready to hear and accordingly provide information about potential interventions and prognosis. This discussion is often iterative and longitudinal given the changing needs of the individual with a dementia syndrome. Tools and video tutorials for making and delivering the diagnosis of dementia are available to clinicians on the ACT on Alzheimer’s webpage.65

Once a diagnosis of dementia is made, there are additional factors that should be assessed and documented. Safety concerns go hand-in-hand with cognitive and functional decline and should be addressed by the primary care provider early on and at follow-up visits to troubleshoot and prevent crises where possible. This includes discussions about medication management, striving to keep regimens as simple as possible with clear communication of changes to caregivers, use of pill box or packs, and avoidance or minimizing medications that could adversely affect cognition further. With cognitive decline comes physical decline, especially if there is underlying parkinsonism or cerebrovascular disease which will increase the risk for falls. Driving is also an important and often contentious topic; however, driving capacity must be discussed openly.66 State-by-state variations in driving regulations and reporting exist and providers should be familiar with those in their own jurisdiction. The American Academy of Neurology has identified strategies to help with decision making on when to advise driving cessation including identifying the stage of cognitive impairment with the Clinical Dementia Rating scale, taking into account caregiver concerns, prior accidents, behavioral symptoms such as impulsivity, an MMSE score of less than 24, and self-reported driving restrictions.67

**COGNITIVE ASSESSMENT BILLING AND CODING**
Driven by the Health Outcomes, Planning and Education for Alzheimer’s Act, Centers for Medicare and Medicaid developed a Current Procedural Terminology code (99483) which provides reimbursement to eligible billing providers for the comprehensive care of patients with dementia. Although Centers for Medicare and Medicaid does not require the use of specific assessment tools, it does require a multidimensional assessment including cognition, function, safety, evaluation of neuropsychiatric or behavioral symptoms, medication review, and caregiver assessment. The details of this assessment are included in Table 3. It is recommended that this assessment be documented in the form of a care plan that
addresses current needs and recommended community resources available to the patient and caregiver.\(^{68}\)

**PARTNERSHIP AND PROGNOSIS**

Patients, care partners, and primary care providers must work closely with hospital-based and subspecialty providers to prevent crisis-driven management during transitions of care. Clear documentation in the electronic medical record by the primary care provider can be very helpful in communicating the patient’s baseline status and preferences. We recommend documentation of the functional status or stage of dementia. Tools that can be helpful for this include the Functional Assessment Screening Tool (FAST) which describes on a 1 to 7 scale the functional, verbal, and physical abilities of the patient with dementia.\(^{69}\) Documentation of the FAST stage can be helpful for longitudinally tracking progression. We also recommend having a clear outline of the patient’s goals and their surrogate medical decision maker present to avoid unnecessary and nonbeneficial testing in this vulnerable population. This documentation serves as the patient’s voice and can assist social service and palliative and acute care providers when patients are in the hospital setting.

When cognitive impairment is identified, a typical question for the primary care provider, from either the patient of caregiver, concerns prognosis, which, as is the case in many other illnesses, can be challenging to predict. For patients diagnosed with MCI, not all cases are early dementia and progression rates to dementia can vary between 8% and 15% per year.\(^{70}\) Studies of patients with MCI show that progression rates to dementia can vary depending on factors such as the population studied, MCI subtype, functional status, and age.\(^{71}\) The trajectory of dementia is variable depending on the patient and disease factors,\(^{72,73}\) but inevitably the trajectory is one of decline, particularly in the last year of life where there is progressive functional and cognitive decline.\(^{74}\) Various tools have been used to prognosticate in dementia, probably the best known of which is the FAST, which can also be used to assess hospice eligibility in AD.\(^{69,75}\) The primary care provider is perfectly positioned to begin goals of care discussions and introduce the role of palliative care in dementia. Palliative care focuses on pain and non-pain symptom management, spiritual and psychosocial wellbeing, support for the patient and their caregiver, and goals of care.

An essential part of caring for patients with cognitive impairment and dementia is also caring for the caregiver. Caregiver burden is well described and impacts not only on the health of the caregiver but also on the patient with dementia themselves in terms of time to institutionalization, behavioral symptoms, and abuse.\(^{76,77}\) Innovative care models, including but not limited to developing care plans and

<table>
<thead>
<tr>
<th>Clinical domain</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Assessment of cognition</td>
<td>Pertinent history and examination</td>
</tr>
<tr>
<td>Functional assessment</td>
<td>Capacity to perform basic and instrumental activities of daily living</td>
</tr>
<tr>
<td>Stage of dementia</td>
<td>Functional Assessment Screening Tool or Clinical Dementia Rating</td>
</tr>
<tr>
<td>Medication review</td>
<td>Medication reconciliation and minimization of high risk medications</td>
</tr>
<tr>
<td>Neuropsychiatric symptoms</td>
<td>Burden of symptoms such as hallucinations, delusions, apathy, depression, and agitation</td>
</tr>
<tr>
<td>Safety evaluation</td>
<td>Discussion of driving capacity, financial capacity, and risk for abuse</td>
</tr>
<tr>
<td>Caregiver assessment</td>
<td>Recognition of caregiver needs and connection to community-based services such as caregiver coaching and respite care</td>
</tr>
<tr>
<td>Advance care planning</td>
<td>Identification of a surrogate decision maker; discussion, and documentation of health care preferences at current and future states of function</td>
</tr>
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Elements may be evaluated in one or more visits. This code should not be reported more frequently than once every 180 days.
education and psychosocial interventions have been developed and proven successful in improving health outcomes and reducing caregiver burden. Although not commonplace yet, there is an impetus to make these models more widely available.

INITIATION OF PHARMACOLOGIC THERAPY

Discussion of pharmacologic treatment options may be undertaken at the time of initial or subsequent cognitive assessment visits. Two main classes of medications are available for the promotion of cognitive and global functioning: acetylcholinesterase (AChEI) inhibitors and memantine. Although comprehensive review of pharmacologic options is beyond the scope of this review, clinicians must be aware of the risk, benefits, and limitations of these medication classes to partner with patients and their caregivers when making treatment decisions.

Acetylcholinesterase inhibitors such as donepezil, galantamine, and rivastigmine increase the concentration of acetylcholine through the reversible inhibition of its hydrolysis by acetylcholinesterase. These medications are indicated for all stages of AD and Parkinson disease dementia (rivastigmine). A recent meta-analysis of patients with AD treated with donepezil compared with placebo showed improved cognitive function as measured by a mean reduction of 2.67 (95% CI, -3.31 to 2.02) on the Alzheimer’s Disease Assessment Scale which ranges in score from 0 to 70 and a mean improvement of 1.05 (95% CI, 0.73 to 1.37) on the MMSE which ranges in score from 0 to 30. Health care use, behavioral symptoms, and quality of life were not impacted by donepezil treatment in this study. Common side effects from AChEI include gastrointestinal effects as well as bradycardia, heart block, and syncope. A recent Choosing Wisely recommendation from the American Geriatrics Society suggests that patients treated with AChEI be assessed for perceived cognitive benefits and adverse gastrointestinal effects regularly, and if desired effects are not perceived, the medication should be discontinued. A meta-analysis of 16 AChEI trials identified that for one patient to benefit, the number needed to treat was 7 for stabilization or better, 12 for minimal improvement or better, and 42 for marked improvement. For one additional person to have an adverse effect, the number was 12.

Data suggest that patients with dementia with Lewy bodies and dementia due to PD may experience comparatively greater benefit than those with AD. In their 2015 meta-analysis, Wang et al found that this medication class enhanced cognitive function, reduced behavioral symptoms, and slightly improved global impression of change.

Memantine is the other US Food and Drug Administration-approved medication for moderate to severe AD. This medication is proposed to be neuroprotective due to the blocking of excessive N-methyl-D aspartate stimulation. Pooled data suggests small clinical benefit for memantine versus placebo when cognitive function and global clinical ratings are measured. This medication does not appear to benefit patients with mild dementia. Common side effects include dizziness, headache, and gastrointestinal symptoms.

CONCLUSION

Dementia remains at the forefront of global public health challenges facing modern society. As the most prevalent cause of disability in older adults, its impact is substantial and far-reaching, posing a significant financial burden on family care partners and the health care delivery system. In this clinical review, we have proposed a systematic, practical, evidence-based approach to managing the patient with new cognitive symptoms in the ambulatory care setting, outlining recommendations for clinical assessment, cognitive testing, imaging, psychosocial concerns, advance-care planning, and pharmacologic options. A critical step is making the diagnosis in a timely manner so that multidisciplinary, patient-centered, and proactive care can ensue. Primary care providers are in a unique position to partner with patients, caregivers, and community supports to deliver high-quality care and prevent crisis-driven management for people with dementia.
Abbreviations and Acronyms: AChEI = acetylcholinesterase inhibitor; AD = Alzheimer disease; CSF = cerebrospinal fluid; CT = computerized tomography; DSM = Diagnostic and Statistical Manual of Mental Disorders; FAST = Functional Assessment Staging; MCI = mild cognitive impairment; MRI = magnetic resonance imaging; NCD = neurocognitive disorder; PD = Parkinson disease

Potential Competing Interests: The authors report no competing interests.

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REFERENCES


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