Office- and Bedside-based Screening for Cognitive Impairment and the Dementias

Which Tools to Use, Interpreting the Results, and What Are the Next Steps?

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KEYWORDS

• Dementia • Cognitive screen • MMSE • MoCA • Mini-Cog

KEY POINTS

- Detection of early cognitive impairment can prevent safety problems and allow treatment for potentially treatable sources of cognitive impairment.
- Choice of a cognitive screen depends on the evidence base of the test, patient population, time constraints, and clinician familiarity.
- Standardized administration of cognitive screens is an essential base to interpretation and diagnostic accuracy.
- Cognitive screens are influenced by non-neurologic factors (eg, education level, age, psychiatric illness, and sensory deficits), which need to be considered when interpreting scores.

INTRODUCTION

The aging population contains increasing rates of cognitive decline and dementia.[1] Cognitive deficits are associated with a variety of neurologic, medical, and psychological conditions, including degenerative dementing illnesses, and other diseases that may negatively impact brain function (eg, diabetes, some cancers, liver disease, stroke/cerebrovascular disease, cardiac conditions, depression, and anxiety), metabolic conditions, endocrine states, medication side-effects, and delirium/encephalopathies. Some of these conditions are reversible with treatment. Although others do not respond to treatment, correct diagnoses may lead to potential resources and care for

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the patient and their caregivers. Health care providers are often the first source patients look to for guidance with cognitive impairment.

An early question for the provider is whether to screen for cognitive impairment. The answer is clearly affirmative when patients or family members present with cognitive concerns or when the provider observes behavior suggestive of cognitive impairment. It is much less clear whether to screen patients without cognitive concerns or symptoms. Recently, the US Preventive Services Task Force[2] recommended that cognitive screening not be completed with non-symptomatic patients, concluding that, "the current evidence is insufficient to assess the balance of benefits and harms of screening for cognitive impairment in older adults (page 757)." Reasons for the decision included the lack of efficacy of treatments for cognitive impairment, especially for non-demented adults, and the poor positive predictive value of screening instruments when used with nonclinical community samples. The Centers for Medicare and Medicaid Services require investigation of cognitive impairment at the annual wellness visit. Although formal cognitive screening is not required, it is suggested as a possibility. The investigation may also be done by direct observation and considering the concerns of friends and family members. Indeed, much information can be gathered using informal methods, such as by asking patients about current events (weather, sports, local events), inquiring about whether medications are properly and consistently used, and asking family members or friends about the patient's daily function skills (eg, medication management, bill paying, driving) and general cognitive status.

Health care workers may feel uncomfortable discussing cognitive matters with patients, and what does not get asked may go unnoticed. Chodish and colleagues[3] found that physicians were not aware of 40% of their patients with cognitive impairment, most likely because they did not investigate the matter. The lack of investigation of potential cognitive deficits may lead to significant safety concerns (eg, poor medication management, driving difficulties) and undertreatment of potentially treatable sources of cognitive impairment.

ASSESSMENT

An ideal cognitive screen will correctly identify patients with cognitive impairment while not pathologizing normal cognition, and will do so in a brief, time-conscious manner. There are numerous cognitive screens available and there is no one-size-fits-all "best" cognitive screen. Choosing a cognitive screen will depend on the patient population, individual patient characteristics, and clinical judgment. Ease of use, time constraints, and evidence of test accuracy will also influence screening tool selection. The following summary highlights three commonly used standardized cognitive screeners.

The Mini-Mental State Examination

The mini-mental state examination (MMSE) is a 30-point cognitive screen that takes approximately 5 to 10 min to administer.[4] It includes questions of orientation, verbal memory registration and short delayed recall, working memory, language, and visuospatial abilities. A cutoff of 23 points or lower is often used as a dementia proxy. The MMSE was originally developed for detecting dementia in a geriatric population and differentiating dementia from other causes of cognitive decline, such as depression.

The MMSE functions best when used for its intended purpose with older adults suspected of dementia. For detecting the presence of dementia in community and primary care samples, scores less than or equal to 24 produce an .87 sensitivity and .82 specificity.[5] Using an education-corrected cut point significantly improves

sensitivity but results in more patients without cognitive impairment being sent for further diagnostic testing.

MMSE is less sensitive to mild cognitive changes, such as those seen in mild cognitive impairment (MCI). Meta-analysis of MMSE detection of MCI versus normal controls indicated scores 27 and below optimized sensitivity and specificity.[6] However, use of higher cutoff scores may result in higher rates of false-positive errors, as MMSE scores can be influenced by other factors (eg, age, education level; see interpretive considerations below).

MMSE content is heavily weighted with orientation and language items and has been criticized for poor sensitivity for executive functioning and visuospatial deficits, which are more common in non-Alzheimer's pathology, such as Parkinson's disease and vascular changes. MMSE has ceiling effects that limit its ability to detect MCI and dementia due to Parkinson's disease.[7] Even with adjusting MMSE scores to higher cut points to improve sensitivity, MMSE is less sensitive than the Montreal Cognitive Assessment (MoCA) in detecting cognitive deficits in recall, executive functioning, abstraction, and sustained attention in patients with transient ischemic attacks and stroke.[8]

Montreal Cognitive Assessment

The MoCA was developed as a screening instrument sensitive to early cognitive declines found in MCI.[9] The MoCA test is 30-point screen and takes approximately 10 to 12 min to administer with items covering eight general domains: visuospatial/executive abilities, naming, memory registration (not scored), attention/working memory, abstraction, memory recall, and orientation. An education correction of one additional point is added for patients with $\leq$12 years of education. Scores $\leq$25 indicate cognitive impairment. Although originally developed to detect prodromal Alzheimer's disease, MoCA has been validated in detecting cognitive impairment of various etiologies, (including Parkinson's disease[10]), vascular cognitive impairment,[11] and other medical conditions.

The optimal MoCA cutoff score is often debated due to concerns for high rates of false-positive errors. Numerous studies have developed optimal cutoff scores for specific populations. For example, Waldron-Perrine and Axelrod[12] recommend an optimal cutoff of $\leq$20 for an urban veteran sample, but a low cutoff would be insensitive in other settings. Meta-analysis revealed that an optimal cutoff of less than 23 optimized diagnostic accuracy.[13] Landsheer[14] examined optimal cutoff scores for detecting cognitive impairment using MoCA and found scores between 22 and 25 were most error-prone for interpretation. Instead of a dichotomous interpretation, using two-threshold points (ie, >25 normal; 22–25 uncertain; <22 is impaired) allows providers to apply a more cautious clinical approach to individuals in the uncertain range and avoid overdiagnosis.

The MoCA and MMSE are both 30-point screens but cannot be used interchangeably. When both the MoCA and MMSE were administered in a sample of poststroke or TIA patients, 58% of participants with normal MMSE scores had impaired MoCA scores.[8] Several studies have created "crossover" tables to convert a score on the MMSE to a score on the MoCA to help clinicians interpret scores [for example,[15]]. In general, MoCA is preferred for detecting subtle cognitive changes of various etiologies but should be interpreted with caution as to avoid over-pathologizing cognitively intact individuals.

Mini-Cog

The Mini-Cog[16] is a brief screen that takes approximately 3 to 5 min to administer. It combines two commonly used tasks—three-word memory and clock drawing—to

measure memory and executive functioning. Each section is worth three points for up to six total. The Mini-Cog was originally developed to screen for dementia in non-white and low-education populations and has been further validated in US population-based samples.[16] The advantages of the Mini-Cog are the ease of use, brevity, and fewer effects of social factors on scores (eg, education level). A Cochrane review of Mini-Cog accuracy in the primary care setting found limited sensitivity and specificity values for detecting all-cause dementia (.76 and .73, respectively), which led to the lack of support for its use in primary care.[17] The Mini-Cog diagnostic accuracy may be improved significantly by adding measures of functioning, such as the Functional Activities Questionnaire (FAQ).[18]

Other Cognitive Screens

Other cognitive screens with adequate psychometric properties include the Addenbrooke's Cognitive Examination-Revised (ACE-R),[19] Memory Impairment Screen (MIS),[20] and General Practitioner Assessment of Cognition (GPCOG)[21] (details in **Table 1**). A disadvantage of the ACE-R is an administration time of approximately 16 min as opposed to MIS and GPCOG, which take less than 5 min. Newer cognitive screens are frequently being developed. Generally, the choice of the cognitive screen will be influenced by its evidence base, appropriateness of use in primary care settings, and clinician's preference.

APPROACH

Administration and Interpretation of Cognitive Screens

Test examination

The choice of a particular screening test is not as important as the ability to competently administer, score and interpret the chosen test. Most cognitive screening tests include standardized administration directions. For example, the MoCA includes specific, word-for-word instructions found on the MoCA website (mocatest.org), and a certification program. The instructions need to be closely followed. When tests are not given in a standardized manner, it hinders the reliability and validity of the results. For example, if two examiners complete the MoCA using different directions, inter-rater reliability suffers. Similarly, if an examiner completes a screening test on two separate occasions with a patient without consistent directions, test-retest reliability is harmed. Because there is a direct relationship between test reliability and test validity, when test reliability suffers it directly and negatively impacts test validity. Therefore, examiners are strongly encouraged to read through administration directions and practice with non-patient volunteers before administering tests to patients. In addition, when there are multiple examiners in a single practice, it is important that they communicate with each other about test administration issues to ensure the test is administered to patients in a consistent manner across examiners. Finally, it is important to score screening tests accurately. To ensure accurate and consistent scoring, consider having both a primary test scorer and a separate score checker; scoring the test twice and checking for scoring consistency increases scoring accuracy.

Test interpretation: age and education effects

Screening tests, like all cognitive tests, are related to patient-related variables. For example, Ylikoski and colleagues[22] found significant education and age-related variance with the MMSE in their Finnish community sample; the two demographic variables accounted for 10% of the MMSE score's variance in the sample. Correcting the MMSE score for age and education improved the accuracy of the study's MMSE-based dementia diagnoses.

Table 1
Common cognitive screens, domains assessed, and recommended interpretive cutoffs

Test	Administration Length (min)	Cognitive Domains Assessed	Score Ranges	Interpretation (Cutoff for Impairment)
Mini-Mental State Examination (MMSE)	5–10	Orientation Verbal memory registration Memory recall Working memory Language Visuospatial abilities	0–30	≤ 23
Montreal Cognitive Assessment (MoCA)	10–12	Visuospatial/executive Naming Memory registration (not scored) Attention/working memory Abstraction Memory recall Orientation	0–30	≤ 25
Mini-Cog	3–5	Memory Executive functioning	0–6	< 3
Addenbrooke's Cognitive Examination-Revised (ACE-R)	12–20	Attention/orientation Memory Fluency Language Visuospatial	0–100	≤ 88
Memory Impairment Screen (MIS)	4	Memory – free recall and cued recall	0–8	≤ 4
General Practitioner Assessment of Cognition (GPCOG)	2–5[a]	Time Orientation Executive functioning Information Memory Recall Informant Report Section	Patient: 0–9 Informant: 0–6 Total: 0–15	Patient: < 8[a] Informant: < 5 Total: < 11

[a] A two-stage method is used: patients with scores greater than 8 or less than 5 are considered intact and impaired, respectively, and the informant section is not administered. Patients scoring 5 to 8 have the informant section administered.

Rossetti and colleagues[23] completed a normative study with the MoCA in a sample of ethnically diverse community adults. Mean MoCA total scores ranged from 25.2 in persons younger than age 35, to 21.3 in persons from age 70 to 80. Moreover, the 70- to 80-year-old subjects with less than a high-school education earned a mean MoCA score of 16.1, which is approximately 10 points below the recognized MoCA cut score. Other normative studies have shown significant education and age effects with the MoCA, suggesting that the cut score may be too stringent, leading to incorrect classification of patients as cognitively impaired.[24]

In addition to the length of education, the clinician should examine the quality of their patient's education. Education quality in the United States has been lower for many African-American and Hispanic-Americans, especially for African-American elders who were educated in the Southern United States. This has led to differences in performance on cognitive tests, including performance on cognitive screening tests.[25]

Why is age inversely correlated with cognitive performance on screening tests? One potential reason is normal cognitive aging. As persons age, they commonly show a mild cognitive decline, especially in such areas as attention, executive functions, and episodic memory.[26] The causes of normal cognitive aging are not clear; to date, studies have been largely unsuccessful in showing robust and consistent relationships between age-related brain changes (eg, white matter hyperintensity, diffuse atrophy) and age-related cognitive decline.

A second potential reason for age-related effects on cognitive screening tests may be increased risk for previously undetected degenerative disease in older versus younger community participants. Age is a strong risk factor for dementia. It may be that older persons in a community sample were at greater risk than younger persons in the sample to have non-detected, early Alzheimer's disease or other degenerative dementia.

Reasons for the direct relationship between education length/quality and performance of elderly subjects on cognitive screening tests may include a person's facility with being in an assessment situation, their ability to complete verbally-based instruction, and cognitive reserve. Cognitive reserve is the hypothesized relationship between brain development and cognitive skills. It is thought that longer periods of high-quality education experiences result in the brain's ability to find alternative ways to complete cognitive tasks when faced with neuronal damage.[27] It may be that persons with longer periods of high-quality education have the ability to overcome some of the negative brain effects of aging, such as diffuse brain atrophy. Cognitive reserve may even provide clues as to how some persons carry significant Alzheimer's-related pathology burden and yet remain cognitively healthy.

To summarize, the clinician who is interpreting a cognitive screening test score must take into account the age and education of the patient. Education should be examined in terms of length and quality. The strength of relationships between aging and education and screening test performance are especially apparent on the MoCA but may also be seen to a lesser degree with the MMSE. Mini-Cog scores have shown a less consistent relationship with age and education than either the MoCA or MMSE.

Test interpretation: effects of psychiatric illness

Depression and anxiety symptoms have consistently been shown to exert mild but significant effects on neuropsychological tests, including cognitive screening tests.[28] Other studies (eg,[29]) have shown that patients with mood disturbance performed worse than non-depressed control subjects on neuropsychological tests, especially on measures of memory and executive function. Del Brutto and colleagues,[28] in a sample of rural Ecuadorian elders, showed that persons with self-reported elevated

depression earned significantly lower MoCA scores than non-depressed individuals, and similar findings have been shown in samples of subjects with diagnosed "severe mental illness.[30] In an electroconvulsive treatment (ECT) study, Obbels and colleagues,[31] showed improvements in MMSE score that corresponded with improved mood measures during and after ECT treatment in a sample of 159 patients, aged 55 and older.

Clinicians need to be alert to the mild but significant effects that mood disturbance and other psychiatric illnesses may have on cognitive screening test results; scores that are 1 to 2 points below expected cut-offs may have been influenced by psychiatric symptoms/illness. Explaining this to patients who score below the cut score may lower their concern that they have a dementing illness. Clinicians may also assure the patient that they will continue to monitor the patient's cognitive status with periodic rescreening to confirm that they are not experiencing a progressive, degenerative condition. Of course, treatment of the psychiatric condition via medication and/or psychotherapy should also be explored.

Test interpretation: medical illness

It is not surprising that persons with diagnosed neurologic conditions often score below standard cut points on cognitive screening tests, because these scores may directly reflect neurologic damage caused by the disease. These include, for example, patients diagnosed with Parkinson's disease, stroke, epilepsy, migraine, multiple sclerosis, and other conditions. It may be more surprising that mild cognitive deficits on cognitive screening tests are often noted in patients with a variety of non-neurologic health concerns, including persons with diabetes mellitus.[32] Zhao and colleagues[33] found that patients with diabetes and high levels of glycated hemoglobin (HbA1c) were more likely to decline on MMSE scores than patients with lower baseline HbA1c levels. Patients with other medical disorders, such as chronic kidney disease,[34] congestive heart failure, and atrial fibrillation,[35] and chronic obstructive pulmonary disease (COPD;[36]) also show lower scores than persons without medical illness. Persons with chronic pain, such as that which is associated with arthritis and fibromyalgia, may also present with cognitive complaints and can be expected to score mildly below established cut-points on cognitive screening tests.[37]

Why should medically ill patients score lower on cognitive screening tests? One reason is potential neurologic underpinnings to the cognitive deficits associated with the illness (eg, diabetes, fibromyalgia). Also, significant medical illness may include chronic pain/malaise and/or psychiatric symptoms, which in turn may negatively affect cognitive performance. Often, the mild deficits associated with illness are related to inconsistent attention and focus, which interfere with consistent cognitive processing speed and learning. Indeed, the cognitive patterns seen on full neuropsychological examinations in these patient groups often show mild deficits and variability on measures of attention, executive functions, and learning, whereas retention memory deficits (ie, rapid forgetting) are not often seen.

Test interpretation: miscellaneous

Other factors that may result in lower screening test results include:

1. Patients for whom English is not their primary language. Involving an interpreter increases the potential variability in the testing environment (eg, if the interpreter does not speak the same dialect as the patient), which decreases examiner control of the testing environment, reliability, and validity.
2. Patients with illiteracy. Patients who do not know how to read or write perform more poorly on cognitive testing of all types. Part of this is because some screening tests

require basic literacy (eg, spelling the word, "WORLD" backward and writing a sentence on the MMSE). Perhaps surprisingly, Illiterate patients perform more poorly on both verbal and nonverbal cognitive tests.[38]

3. Patients with sensory deficits. Patients who are hard of hearing or vision impaired often perform poorly on cognitive screening tests. This likely is related to a lack of accurate communication between the examiner and the test taker, but it also may be because standardized test administration is necessarily altered.
4. Patients with inconsistent test engagement or effort. Some patients do not wish to be tested and do not put forth consistent effort during test examination. Other patients may have an incentive to perform poorly. Clinicians need to be alert to the potential that a patient may see it as in their best interest to perform poorly on a screening test.
5. Practice effects. Although most other factors in this section are related to poorer than average test performance, practice effects result in a patient's performance being artificially elevated. To guard against practice effects, consider using multiple forms of a test (eg, both the MoCA and the Mini-Cog have multiple versions and the MMSE allows for alternative words for learning and recall).

SUMMARY

A Proposed Four-Step Clinical Plan for Patients with Cognitive Concerns

Cognitive screening may be part of a more comprehensive plan for assisting patients with cognitive concerns. The first step of the plan is *education*. When patients bring up cognitive concerns, it is important for clinicians to educate them, especially about normal cognitive aging. Patients should be informed that some mild cognitive change is common, especially in the areas of new learning, attention, and memory. Informing them of the likely normality of their concerns can be reassuring. Other areas of education include the potential roles that depression and anxiety, as well as other psychiatric symptoms, may have in cognitive deficits.

The second step in treating patients with cognitive concerns is *screening*. Choose a screening test that you have time to administer and are comfortable with. Learn to interpret screening results, including how factors introduced in the previous section may influence the obtained screening test score. There are, of course, many different screening test options. We chose to review the MMSE, MoCA, and Mini-Cog because of their frequency of use and the availability of psychometric data. When choosing a screening test, consider choosing the MMSE when evaluating an elderly person for the presence of a dementing illness, especially in situations where false-positive errors (stating that there is cognitive impairment when there is none) are more costly than false negative errors (stating that there is not cognitive impairment when cognitive impairment exists). Consider choosing the MoCA in younger patients, especially in patients with adequate years of quality education, and in patients for whom an evaluation of executive functions is important. As mentioned, the MoCA provides greater sensitivity than the MMSE, but at the cost of lower specificity. Finally, in situations where it is not possible to spend the necessary time for the MMSE or MoCA, consider the Mini-Cog to provide a first look at basic cognitive abilities.

The third step in this process is *follow-up*. After you complete the screening test, educate your patient on how they did and whether follow-up tests are indicated. Follow-up tests may include laboratory tests for potentially reversible causes of cognitive decline. If the patient provides permission, follow-up may also include speaking with their spouse or family members to see if they have noted a decline in cognitive

or functional abilities. If depression or anxiety symptoms are significant enough to interfere with everyday life, treatment, such as medications and/or psychotherapy, should be discussed with patients. Finally, let your patient know that you may wish to screen them again for cognitive deficits at a future visit to see if there are changes in cognitive abilities over time. Longitudinal cognitive data is an important potential source of information of possible degenerative cognitive conditions.

Finally, the fourth step is a potential *referral*. You may wish to refer the patient to specialists for additional assessment. This may include neurologists or neuropsychologists for a more comprehensive cognitive and functional assessment. Other specialists may also be able to assist, depending on the results found in your cognitive assessment, and the questions they may raise.

The overall goal for assessment and treatment of your patient's cognitive concerns it to improve your and your patient's understanding of their cognitive condition and to provide assistance with potential treatment and resources. Cognitive screening tests have an important role in this process, and when used properly, greatly improve the care of patients with cognitive concerns.

CLINICS CARE POINTS

- Each cognitive screening test has strengths and weaknesses, and the clinician should choose the test that works best in their clinic
- Cognitive screening tests need to be administered and scored in a standardized manner to not detract from their reliability and validity
- Age, education (length and quality), psychiatric illness, medical illness, effort, illiteracy, and sensory deficits may have significant effects on patients' performance on cognitive screening tests
- Cognitive screening should occur along with education, follow-up, and targeted referrals for effective care of patients with cognitive concerns

DISCLOSURE

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