Received: 16 July 2024 | Revised: 19 September 2024 | Accepted: 21 September 2024

DOI: 10.1002/alz.14335

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

PERSPECTIVE

The Alzheimer's Association clinical practice guideline for the diagnostic evaluation, testing, counseling, and disclosure of suspected Alzheimer's disease and related disorders (DETeCD-ADRD): Validated clinical assessment instruments

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Funding information
Alzheimer's Association

Abstract

US clinical practice guidelines for the diagnostic evaluation of cognitive impairment due to Alzheimer's Disease (AD) or AD and related dementias (ADRD) are decades old and aimed at specialists. This evidence-based guideline was developed to empower all—including primary care—clinicians to implement a structured approach for evaluating a patient with symptoms that may represent clinical AD/ADRD. As part of the modified Delphi approach and guideline development process (7374 publications were reviewed; 133 met inclusion criteria) an expert workgroup developed recommendations as steps in a patient-centered evaluation process. The workgroup provided a summary of validated instruments to measure symptoms in daily life (including

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cognition, mood and behavior, and daily function) and to test for signs of cognitive impairment in the office. This article distills this information to provide a resource to support clinicians in the implementation of this approach in clinical practice. The companion articles provide context for primary care and specialty clinicians with regard to how to fit these instruments into the workflow and actions to take when integration of performance on these instruments with clinical profile and clinician judgment support potential cognitive impairment.

KEYWORDS
Alzheimer's disease, cerebrospinal fluid, dementia, diagnosis, frontotemporal dementia, Lewy body dementia, magnetic resonance imaging, mild cognitive impairment, molecular biomarkers, positron emission tomography, vascular cognitive impairment

1 | INTRODUCTION

The Alzheimer's Association convened a Diagnostic Evaluation, Testing, Counseling and Disclosure Clinical Practice Guideline Workgroup (the DETeCD-ADRD CPG Workgroup). Our emphasis is on good clinical practice for the process of evaluating a patient presenting with an illness (i.e., symptoms, obtained through history, and signs, obtained through examination) that may represent the clinical manifestations of common brain diseases, especially Alzheimer's disease (AD) and AD related dementias (ADRD)—in some cases with exacerbating medical conditions or factors. While this guideline applies to a patient with any severity of cognitive or behavioral impairment, it does not consider individuals who do not have symptoms; therefore, it does not address the topic of screening in asymptomatic people.[1–6] This DETeCD-ADRD CPG seeks to empower all clinicians, including those in primary, specialty, or subspecialty care, to implement a structured yet individualized patient-centered approach to diagnostic evaluation that includes clear communication with the patient and an informant or care partner(s).

For any given individual, differentiation of what is a cognitive–behaviorally impaired versus an unimpaired state requires clinical judgment.[2,7–12] The determination that a person has mild cognitive impairment (MCI) or dementia (or Mild versus Major Neurocognitive Disorder in Diagnostic and Statistical Manual of Mental Disorders Fifth Edition terminology) is the first step of a diagnosis that requires the clinician to integrate reliable history regarding the types and trajectory of changes in cognitive, activities of daily living (ADL), and mood and behavioral functions (from the individual and an informant) with the patient's performance on tests of cognitive function in multiple domains (attention, memory, language, executive function, visual function, socio-emotional behavior).[7–9] The reported symptoms and performance on tests are both influenced by a variety of individual factors that have to be considered, including education, occupation, culture, living situation, family or other relationship dynamics, developmental history, and medical and psychiatric comorbidities.

For example, the diagnosis of dementia may be straightforward in a formerly high-functioning patient whose family reports insidious onset of impaired memory and executive function with impairment in instrumental activities of daily living (IADLs) and who scores a 20/30 on the Montreal Cognitive Assessment (MoCA).[13] Yet this first step in the diagnostic formulation may be very challenging in a symptomatic and highly educated person who reports memory loss with an impact on occupational function but who performs in the unimpaired range on a brief cognitive assessment test like the MoCA; such an individual may require a neuropsychological evaluation to document impaired performance or to establish a current baseline that can serve to track changes. Unlike the diagnosis of anemia, hyperkalemia, or proteinuria, there is no test value that determines the diagnosis of MCI or dementia—it requires integration of multiple layers and types of information and, importantly, clinical judgment.

In some cases, a patient with cognitive concerns may be documented to perform normally on detailed neuropsychological evaluation; such a person might be classified as having "subjective cognitive decline," a clinical construct being studied extensively by an international research community.[14] In other cases, a patient has developed an acquired change in personality or behavior but is found to be cognitively intact; such a patient might be classified as having "mild behavioral impairment," another clinical construct being evaluated by the research community.[15–18]

The second step—determination of cognitive–behavioral syndrome—facilitates communication about the specific types of impairments the patient has, regardless of the severity of those impairments (i.e., MCI or dementia). While some patients present classically with one of the recognizable cognitive–behavioral syndromes (see Table 2 of companion manuscript),[19] others may not fit so clearly into these syndromic diagnostic criteria. In these cases, additional information from informants may be helpful, or additional office-based assessments of cognitive, behavioral, and sensorimotor function may be necessary, or consultation with a specialist(s).

1.1 | History of present illness

Regardless of whether the patient or a family member initiated the medical contact, the history of present illness (HPI) is the cornerstone of the approach to medical diagnosis. In the era of the electronic

medical record in which more activities are relegated to templates and checkboxes, the artful elicitation of the HPI is an interactive exercise in spontaneity, unexpected responses, and nimble redirection. In practice, the initiation of an evaluation for cognitive or behavioral concerns, particularly when symptoms are relatively more prominent, is more likely to have come from a family member or close friend rather than the patient, because of the impairment or loss of awareness and insight that often accompany acquired cognitive and behavioral syndromes. The family member or friend who often prompts the evaluation becomes a confidante or "informant" who provides key observations to the clinician, who should compassionately elicit, compile, and ultimately integrate and interpret what the patient and informant(s) describe. A substantial body of evidence indicates that—in the setting of what ultimately is diagnosed as a likely neurodegenerative form of MCI or dementia—informant reports provide added value to the history as taken from the patient[20–25] and to cognitive test performance.[25–28]

The goal is to obtain a comprehensive description of the patient's principal cognitive and behavioral symptoms and their impact on daily function, interpersonal relationships, and comportment; the time course of those symptoms; the existence and evolution of other relevant symptoms; and the pertinent medical history and risk factors. The interaction between historian (i.e., the clinician) and the patient and informant(s) almost always begin with the query that has the general form: "What is the main reason you are here to see me and what would you like to accomplish from the visit today?"

1.2 | History of cognitive symptoms

In the context of a suspected cognitive–behavioral syndrome in an older adult, the potential for complexity, ambiguity, or misdirection of the response to this question is predictably unpredictable. Because diminished insight is common in individuals with a syndrome of cognitive–behavioral impairment, the patient and their care partner (informant) may have divergent opinions about the nature of the symptoms and their consequences. The likelihood of a potential disagreement in perspectives can be communicated up front and be acknowledged as a useful clue for the clinician (e.g., "This is a safe place and time when you should feel free to disagree with each other: it can help me understand and advise you better"). It may be valuable to interview the patient and informant(s) separately because of discomfort with honest reporting or overt friction. Therefore, the clinician needs to be flexible and to encourage and pursue all lines of the story and, informed by these and other information gathered during or after the visit (post-visit phone calls are often helpful), integrate perspectives and information into an initial narrative that represents the most likely approximation of the actual events.

The meaning of words like "memory loss" or "confusion" used by the patient and informant may differ substantially from the clinician's sense of those words. The clinician must therefore encourage the patient or informant to elaborate by giving specific examples. The loss of episodic memory that occurs in typical MCI or dementia due to AD involves difficulties with learning and recalling newly acquired information and recent life events. Sometimes patients or informants may use the term "memory loss" when referring to word-finding difficulty, inattention, loss of geographic orientation, or loss of the ability to perform step-by-step tasks. It can be very challenging to distinguish the early stages of cognitive decline due to neurodegenerative disease from normal aging. It is important to skillfully communicate that changes which may be common in individuals with advancing age are not always normal and could benefit from further diagnostic evaluation. Several validated instruments offer structured questionnaires to assist in the organization and reporting of symptoms of cognitive impairment (some of these also include mood/behavior and/or daily function (Table 1)).

A critical element of the compilation of a history of cognitive or behavioral symptoms is its profile of characteristics, intensity, temporal course, and impact. Patients and informants may struggle to explain how symptoms first appeared; how they may have evolved over time in frequency, duration, and intensity; or whether the symptoms were episodic or ever-present but may have become more noticeable or troubling. It is very common for patients and companions to frame their history-telling around an event such as a surgery or a major psychosocial trauma that they concluded was solely causal. It can be very challenging for a clinician to dissociate the description of symptoms or behaviors of the patient from the patient's or care partner's view of a possibly (but in many cases not likely solely) causal mechanism. Patients, informants, and many clinicians with limited proficiency with dementia assessment often attribute changes in cognition, daily activities, behavior, or sensorimotor function to "normal aging" or to anxiety, mood, or sleep disorders. While acquisition of some of the critical historical information could be captured using algorithmic approaches, the clinician's understanding of a history of the insidious development of mid- to late-life cognitive or behavioral symptoms is an iterative process, truly an art anchored in clinical experience, diligence, and judgment. Proficiency in this art can be facilitated by a comprehensive and structured approach, but for it to be patient centered and most beneficial, this triadic dialogue, which also provides ample opportunities for psychoeducation, cannot be reduced to an algorithmic inquisition.

1.3 | History of mood and/or behavioral symptoms

In many patients, behavioral or mood-related (neuropsychiatric) symptoms are an early feature of neurodegenerative disease and may or may not be recognized by patients or informants as part of the illness under evaluation.[46,47] In many cases, the patient or care partner may not recognize them as being related to cognitive decline, a condition or brain disease, and the clinician must probe for these or other neuropsychiatric symptoms. In addition to providing diagnostic information, symptoms such as depression, anxiety, delusions, hallucinations, agitation, or obsessive-compulsive behavior may offer targets for symptomatic treatment. Yet the clinician must also make sure that the words being used by the patient or informant to report on symptoms are consistent with the observed changes in behavior. Concerns about "personality change" need to be discussed to determine whether they arise from apathy, depression, anxiety, hallucinations,

TABLE 1 Validated instruments to assist in the structured reporting of symptoms of cognitive impairment.

Instrument	Purpose	Features	Comments
IQCODE[29–31]	The first informant-based questionnaire to rate change in cognitive function from the person's previous ability.	Original had 26 items; short version has 16 questions that measure cognitive decline from premorbid level. Each item is rated on a 5-point scale from 1 ("much better") to 5 ("much worse") and ratings are averaged, with 3 representing no change. Validated in people with dementia against other measures of cognitive decline. Not influenced by education, pre-morbid ability, or language proficiency, but is affected by informant characteristics and the quality of the relationship between the informant and the subject. Less sensitive to MCI.	Available at https://nceph.anu.edu.au/research/tools-resources/informant-questionnaire-cognitive-decline-elderly Information from the IQCODE and the MMSE can be combined in the DemeGraph (https://biostats.com.au/Demegraph/) to aid in assessing for dementia.
AD8[32]	Brief screening (2–3 minutes) interview that can differentiate between individuals with and without cognitive impairment.	A patient or informant rates yes/no questions about memory, orientation, judgment, and everyday function. The AD8 is a valid and reliable dementia screening measure compared to the expert clinical judgment and neuropsychological assessments. The AD8 is an appropriate screening tool for dementia but may not be sensitive to other more acute or subtle forms of cognitive dysfunction.	Available at https://www.alz.org/media/Documents/ad8-dementia-screening.pdf
QDRS[33]	10 item questionnaire completed by informant, rating change from premorbid baseline on an ordinal scale from 0 to 3, which when summed aim to capture the types and severity of cognitive and behavioral symptoms and impact on daily function.	The QDRS is a free screening and staging tool (not a diagnostic tool). It can be used as a structured screen for cognitive, behavioral, and functional changes and symptoms as well as for staging severity. QDRS scores correlate with the longer CDR (see Table 3). Takes 7-10 min of informant time. Score range interpretations: normal 0-1; MCI 2-5; mild dementia 6-12; moderate dementia 12-20; severe dementia 21-30.	Available at https://umiamibrainhealth.org/downloads/the-quick-dementia-rating-system-qdrs-patient-and-informant-versions/
AQ[34,35]	Developed as primary care tool to detect cognitive impairment due to AD.	The AQ is an informant-based assessment consisting of 21 yes/no questions that can be administered in ≈ 3 minutes. The individual items are divided into the domains of memory, orientation, functional ability, visuospatial, and language. Items that receive a "yes" response are given 1 point; six items particularly associated with clinical AD more weighted and are given 2 points. The total AQ score ranges from 0 to 27; normal ≤4; MCI 5–14; AD dementia ≥15.	Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3207359/pdf/nihms325035.pdf [35]
ECog[36,37]	Assesses functional abilities that are linked to specific cognitive abilities.	39-item questionnaire can be given to informants and separately to patients. Scoring produces one global factor and six domain-specific factors. Subsequent studies support validity of short-form ECog-12 in discriminating against people with dementia from cognitively normal individuals, but less sensitivity for MCI. Validated against other measures of functional and neuropsychological impairment.	The original ECog and ECog-12 are detailed in Farias et al.[36] and Tomaszewski Farias et al.[37]
CFI[38]	The CFI was developed to facilitate evaluation of cognitive symptoms in dementia prevention studies.	14-item questionnaire focused on change in cognitive and functional abilities over the previous year, which is completed by patient or separately by informant. Total scores range from 0 to 14 (yes = 1, no = 0, and maybe = 0.5), with higher scores indicating greater subjective cognitive complaints. In people with MCI, informant rating is useful for prognosis.[39]	Full questionnaires are available in Li et al.[39]

(Continues)

TABLE 1 (Continued)

Instrument	Purpose	Features	Comments
Cognitive Change Index[40]	Originally developed from measures to detect subjective cognitive decline	A 20-item questionnaire asking patients and informants to separately rate change in cognitive function compared to the previous 5 years on a scale of 1 (no change) to 5 (severe change). Questions cover memory, executive function, and language. Validation study showed that scores from informant reports are abnormally elevated in people with MCI or dementia.	Available from the authors upon request.
Cambridge Behavioural Inventory[41–43]	Developed to assist in the differential diagnosis of different forms of dementia.	A 45-item informant-completed questionnaire that obtains information about a range of cognitive, mood and behavioral, and daily functional symptoms. May be best for specialty settings or some general practice settings.	Available at https://www.sydney.edu.au/brain-mind/resources-for-clinicians/dementia-test.html
SIST-M[44,45]	Developed as an interview (≈ 25 minutes) for history of symptoms of cognitive and functional impairment	SIST-M has high reliability against the CDR score in people with MCI and mild dementia. An informant-rated questionnaire has also been developed. Best for specialty settings.	Available in Okereke et al. [44,45]

Abbreviations: AD, Alzheimer's disease; AD8, Eight-item Information nterview to Differentiate Aging and Dementia; AQ, Alzheimer's Questionnaire; CDR, Clinical Dementia Rating; CFI, Cognitive Function Instrument; ECog, Everyday Cognition; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; QRDS, Quick Dementia Rating Scale; SIST-M, Structured Interview and Scoring Tool–Massachusetts Alzheimer's Disease Research Center.

delusions, disinhibition, impulsivity, compulsive behavior, or loss of empathic concern. Similarly, an informant's impression that a patient who is no longer interested in previous activities is depressed might arise when the patient's change in affect and behavior is rather due to apathy and executive dysfunction. A clinician experienced with these problems who carefully probes the history will often be able to differentiate apathy and executive dysfunction from symptoms consistent with major depressive disorder. Correspondingly, reports of the patient appearing anxious, hiding items and then not knowing where they are, being avoidant, and "forgetting" or resisting to take medications or to eat may, upon a deeper dive by a probing clinician, be discovered to be due to paranoid delusions or hallucinations (e.g., see recently updated International Psychogeriatric Association [IPA] criteria for psychosis in major and mild neurocognitive disorders[48]) instead of anxiety and memory dysfunction. The approaches to psychoeducation, counseling, management, and care differ greatly based on these different impressions and conditions.

Neuropsychiatric symptoms often precede cognitive decline, and they commonly increase in frequency and intensity as neurodegenerative dementing conditions progress.[49] The 13-item Neuropsychiatric Inventory (NPI)[50,51] is the most widely used instrument to survey many of these symptoms. Other validated instruments offer structured questionnaires that can assist in the organization and reporting of symptoms of mood or behavioral change (Table 2).

In contrast, some patients present with late age-of-onset depression that may be a primary psychiatric illness (see Box 3 of companion manuscript[19]) or a symptom associated with vascular–ischemic cognitive impairment, prodromal Parkinson's disease, or other conditions not necessarily related to a progressive disease leading to dementia. It can be very difficult to differentiate these clinical depression syndromes from a dementia-related syndrome with accompanying depression. More in-depth assessment instruments used to evaluate depression include the Geriatric Depression Scale (GDS),[60] Patient Health Questionnaire 9 (PHQ-9),[56] or Cornell Scale for Depression in Dementia (CSDD).[61,62] In patients with challenging and complex profiles, formal neuropsychological evaluation can be particularly helpful to assess potential contributions of depression or mood disorders to cognitive–behavioral symptoms and performance, and to aid in the differential etiological diagnosis as well as recommendations for next steps in evaluation and care.

1.4 | The impact of cognitive or behavioral symptoms on IADLs and ADLs

Impairment in daily functioning is a core element of the diagnosis of dementia. The patient and informant should be queried about aspects of daily functioning that might be affected by impairments in the domains of learning and memory, language, attention, executive functioning and mental agility, spatial cognition, and psychomotor speed. In a patient with cognitive complaints, the clinician should carefully survey for examples of success or difficulty with complex IADLs. The survey of ADLs should include advanced ADLs[63–65] (e.g., management of financial matters, hobbies/work, technology, leisure, travel to unfamiliar areas), IADLs (e.g., household tasks such as meal preparation, medication use, driving), and basic self-care activities (e.g., bathing, dressing, toileting). The clinician may ask the informant: "Does she/he (referring to the patient) carry out (then name the specific task)?" If the answer is yes, then ask: "Is it more difficult for her/him (the patient) to carry this out that in the past?" How long has it been since you/your loved one has been able to do (then name the specific, individual functional task that they had previously been able to

TABLE 2 Validated instruments to assist in the assessment of neuropsychiatric symptoms in AD/ADRD.

Name	Format	Considerations
General instruments for neuropsychiatric symptoms		
NPI-Q[51]	12-item questionnaire completed by informant; each item is first rated as "present/absent" (Yes/No); if present, severity is rated on 3-point scale from mild (1) to severe (3). Severity total range: 0–36 (none-max) Symptom Distress (how much it affects informant/care partner): rated on 6-point scale (0–5). Distress range: 0–60 (none-max)	Covers broad range of symptoms/behaviors. It is a modified (abbreviated) version of the NPI. The 12 neuropsychiatric domains assessed are: delusions; hallucinations; agitation/aggression; depression/dysphoria; anxiety; elation/euphoria; apathy/indifference; disinhibition; irritability/lability; motor disturbance (e.g., pacing, picking, repetitive motor behaviors); night-time behaviors; and appetite/eating. Suitable for both detection and tracking progression/monitoring. Provides information regarding severity of symptoms (how noticeable it is in the patient) and the amount of distress it is causing the care partner/informant. Some modified versions (e.g., NACC UDS) only gauge symptom severity. It can take 5 to 10 minutes depending on proficiency of administrator and familiarity of informant and whether both severity and distress are elicited. A total score can also be derived by multiplying severity score and distress score for each item and summing across all items. Available at: https://www.alz.org/media/Documents/npiq-questionnaire.pdf
NPI[52]	12 items administered in a structured interview to informant with ratings similar to those above (NPI-Q)	Requires training and proficiency to administer. Used widely in clinical research and more suitable administration to specialist setting; NPI-Q provides good proxy in clinical setting. Available at: https://www.alz.org/media/Documents/npiq-questionnaire.pdf
BEHAVE-AD[53,54]	25 item scale administered to informant; presence of symptoms and impact on patient for each item rated from 0 to 4 (not present to severe) Global impact severity on care partner/informant is rated for each item from 0 to 4 (not troubling to severely troubling)	Covers broad range of symptoms/behaviors. Mostly used in clinical research setting and more suited to specialist setting; ≈ 20 to 25 minutes to administer; solicits presence of behavioral symptoms and their impact. Suitable for detection, staging, and tracking progression/monitoring.
MBI-C[17]	34-item questionnaire structured to be consistent with the five domains in the MBI criteria: decreased motivation, emotional dysregulation, impulse dyscontrol, social inappropriateness, and abnormal perception or thought content. If a question is endorsed as present, it is rated mild, moderate, or severe.	Questionnaire to be used primarily by family members or other close informants to systematically measure behavioral changes exhibited by older adults that might precede the onset of dementia. It was specifically designed to: (1) operationalize the MBI concept; (2) measure a selected list of neuropsychiatric symptoms which may help identify prodromal illness; and (3) help predict risk of dementia due to AD or ADRD. The primary goal is case detection of a behavioral pre-dementia state not better captured by other diagnostic criteria.
Depression instruments		
GDS[55]	15 items Patient self-administered (but can be administered to patient) Yes/No responses	Quick (3–5 minutes) screening tool for depressive symptoms and depression in older adults, public domain. Scores of 5–8 suggest potential for mild depression; 9–11 moderate depression; 12–15 severe depression. Suitable for detection (and abbreviated monitoring) in MCI and mild dementia. Less suitable for more advanced and severe dementia and individuals with poor comprehension; and for monitoring severe depression.
PHQ-9[56]	9 items Patient self-administered (clinician verified) Each item rated 0–3: 0 = not at all; 1 = several days; 2 = more than half the days; 3 = nearly every day Range 0–27 (no depression–severe depression)	Quick (3–5 minutes) screening, diagnostic, and monitoring tool for depressive symptoms and depression in older adults widely use in primary care. Has been validated in individuals with MCI/dementia Scores of 5–9 suggest mild depression; 10–14 moderate depression; > 14 moderately severe/severe depression. Also available in shorter 4- and 2-item versions. Suitable for detection and monitoring in MCI and mild dementia. Less suitable for more advanced and severe dementia and individuals with poor comprehension. Available download from: https://www.mdcalc.com/calc/1725/phq9-patient-health-questionnaire9

(Continues)

TABLE 2 (Continued)

Name	Format	Considerations
CSDD	19 items Administered to patients and care partner (patient does not need to be able to answer for scale to be completed. Each item rated: 0 = absent; 1 = mild to intermittent; 2 = severe Scores range from 0 to 38 (none–max depressive symptoms)	Well suited for detecting, tracking progression, monitoring depression, and depressive symptoms across severity spectrum of MCI-dementia. Scores of > 11 suggestion probable depression.
Anxiety Instruments		
PSWQ-A[57]	8 items Patient self-administered (can also be administered to care partner/informant) Ratings for each item are on a 1–5 Likert scale (1 = not at all typical of me; 5 = very typical of me) Range 8–40 (no anxiety–severe anxiety)	A widely used abbreviated version of the 16-item PSWQ that was developed as a screening tool to assess worry symptoms and anxiety in older adults. It is in the public domain. Cut-off of 17 has been suggested for detection of significant anxiety in individuals with mild/moderate dementia.[58]
GAI[59]	20 items Patient self-administered (can also be administered to care partner/informant) All items answered dichotomously Yes (1) or No (0) Range: 0–20 (none–max severity)	Was developed to screen for anxiety symptoms in older/geriatric population, has been subsequently studied in mild to moderate AD dementia (a cut off score of 8 has been suggested to detect significant in mild/moderate dementia[58]). Suitable for detection of symptoms. It is copyrighted and fee may be required for clinical use. A short form with five items (GAI-SF) is also available for very brief screening.
Agitation instruments		
CMAI	Presence and frequency of 29 behaviors Does not rate severity Administered to care partner informant.	Broadly covers presence of agitation and related disruptive behaviors such as verbal aggression, repetitiveness, screaming, hitting, grabbing, and sexual advances. Requires training to administer, more suited to specialist setting and clinical research.

Abbreviations: AD, Alzheimer's disease; ADRD, Alzheimer's disease related dementias; BEHAVE-AD, Behavioral Pathology in Alzheimer's Disease Depression Scale; CMAI, Cohen Mansfield Agitation Index; CSDD, Cornell Scale for Depression in Dementia; GAI, Geriatric Anxiety Inventory; GDS, Geriatric Depression Scale; MBI-C, Mild Behavioral Impairment Checklist; MCI, mild cognitive impairment; NPI, Neuropsychiatric Inventory; NPI-Q, Neuropsychiatric Inventory-Questionnaire; PHQ-9, Patient Health Questionnaire; PSWQ-A, Penn State Worry Questionnaire Abbreviated.

accomplish)?' and "What was performance at that time versus now?" This inquiry can solidify the clinician's understanding of the onset and trajectory of change in symptoms. Several instruments have been validated to assess daily function (see Table 3).[66–70] The Functional Activities Questionnaire (FAQ)[71] is one such instrument intended for mildly impaired persons (in the MCI and mild dementia range) that can be completed by an informant in a few minutes and that is widely validated and used in US dementia research centers. The Amsterdam-IADL scale[72] is a more recently developed and rigorously validated[73,74] instrument that shows good discrimination between cognitively unimpaired, subjective cognitive decline, MCI, and mild dementia due to AD[75] and good sensitivity over time.[76] In practice, it may be helpful to ask the patient and an informant to complete one of these instruments and then the clinician can review it and probe further as necessary.

1.5 | Review of cognitive, behavioral, and sensorimotor systems

There may be relevant symptoms not reported by the patient or informant or elicited by the clinician during the HPI that can be identified in a structured review of cognitive and behavioral systems. The absence of such symptoms may also be important pertinent negative findings in the patient history. Validated questionnaire instruments (which can be completed by the patient and/or informant in the waiting room) for surveying a number of cognitive domains include the Everyday Cognition scale (ECog)[23] or Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE).[88–90] A validated instrument for surveying a number of relevant mood/behavioral systems is the NPI Questionnaire (NPI-Q). Other validated instruments capture both cognitive and behavioral systems (e.g., Cambridge Behavioral Inventory,[41,42] Quick Dementia Rating System[33,91]). Dementia subspecialists often rely on experience to ask a comprehensive series of structured questions covering cognitive and behavioral systems not discussed in the HPI; one approach to history-taking and clinical decision-making that aims to bring this into primary care is being disseminated as the California Assessment of Cognitive Complaints Toolkit for Alzheimer's Disease, known as the "California Toolkit," which is freely available on the internet.[92] The National Institute on Aging (NIA) website also contains helpful information, useful assessment tools, and links to resources to facilitate AD/ADRD detection, diagnosis, patient/family education, and clinical care,[93] as does the website for the American Academy of Family Physicians (AAFP).[94]

TABLE 3 Validated instruments to assist in the structured assessment of functional impairment in instrumental and basic ADL in patients with cognitive impairment.

Instrument	Purpose	IADL	BADL	Features	Comments
FAQ[71]	IADLs of older adults in the community with and without cognitive impairment or mild dementia	Yes	No	10 items rated on a 4-point scale ranging from: ''dependent (3), requires some assistance (2), has difficulty but does by self (1), performs task normally (0)'' also category for "not applicable (N/A) or never did"	Useful for initial assessment of IADLs in suspected MCI or mild dementia. Not useful for longitudinal tracking of changes beyond mild to moderate dementia stages. Available at https://www.alz.org/careplanning/downloads/functional-activities-questionnaire.pdf
CDR[77–79]	Geared primarily toward typical AD dementia, the CDR was developed to provide a global clinician-rated measure of the presence and severity of cognitive symptoms and their functional impact.	Yes	Yes	Structured interview and examination approach for the trained (usually specialist) clinician to integrate information from history and brief examination to grade the types and severity of impairment in three domains of cognitive abilities (memory, orientation, and judgment) and in three domains of daily function (community affairs, home and hobbies, and personal care). Global rating indicates very mild (0.5), mild (1), moderate (2), or severe (3) dementia. The CDR Sum of Boxes measure ranges from 0 (cognitively unimpaired) to 18 (severe global impairment).	The CDR is well established as a reliable and valid combined cognitive and functional assessment measure for patients with MCI and dementia due to AD and has been used with patients with ADRD as well. It is widely used as a clinical trial outcome measure and a clinical research staging instrument. It is relatively time consuming and therefore used in a limited fashion in specialty clinical practice settings.
FAST[80–82]	Based on the previously developed Global Deterioration Scale for typical AD dementia,[83] the FAST characterizes a patient's daily function through 16 ordinal stages ranging from cognitively unimpaired to severe dementia.	Yes	Yes	The FAST has been validated in primary and specialty care settings and can be administered by clinical or non-clinical staff. The FAST is administered by interviewing a care partner or the patient if at a mild level of impairment. The description that best fits the person's performance is the stage in which the person is functioning. In typical AD dementia, symptoms progress in sequence. However, atypical dementias may not follow this sequence.	Widely used in geriatric medicine and in the US Veterans Administration Health Care System. Often used as a measure by which to determine preliminary eligibility for palliative or hospice care in patients with severe dementia.
Bristol Activities of Daily Living Questionnaire (BALDS)[84]	Basic and instrumental ADLs in individuals with dementia in most settings	Yes	Yes	20 items Range of 0–60 (independent–dependent) Items rated on a 4-point scale (0,1,2,3).	Useful for initial assessment and tracking of IADLs and BADLs across the spectrum of dementia stages.

(Continues)

TABLE 3 (Continued)

Instrument	Purpose	IADL	BADL	Features	Comments
DAD[85]	Leisure activities, IADLs, ADLs in individuals with dementia of the AD type.	Yes	Yes	40 items (23 IADL items; 17 BADL items) Range of 0%–100% (dependent-independent) Items rated on a 2-point scale (0,1) or N/A; Yes, did activity without reminder or assistance = 1; No did not do activity or needed reminder or assistance for activity = 0; Scores added for all questions not rated N/A and converted to % score	Useful for initial assessment and for tracking of leisure activities, IADLs, and BADLs across the spectrum of dementia stages.
DAD-6[86]	A modified version of the DAD scale focusing on executive components of six instrumental items to detect early impairment in a non-demented population.	Yes	No	18 items in six categories Range of 0–18 (dependent–independent) Items rated on a 2-point scale (0,1) or N/A; Yes, did activity without reminder or assistance = 1; No did not do activity or needed reminder or assistance for activity = 0; Categories: meals; travel; use of telephone/computer; finances and correspondence; drug intake; leisure and household care	Less studied but may be useful for initial assessment of leisure activities and IADLs in suspected MCI. For each category there is a question regarding initiation, organizing and planning, and effective implementation. Not useful beyond mild dementia stages.
Lawton and Brody IADL scale[87]	Instrumental activities of older adults in the community with and without cognitive impairment or dementia.	Yes	No	eight items Range of 0–8 (dependent–independent) for women (and traditionally 0–5 for men) Women are scored on all eight areas of function; historically, for men, the areas of food preparation, housekeeping, laundry have been excluded. Individuals are scored according to their highest level of functioning in each category.	Long history of use. Limited assessment of psychometric properties. May be useful for initial assessment of MCI and dementia. Available at https://www.alz.org/media/Documents/lawton-brody-activities-daily-living-scale.pdf
A-IADL-SV[75]	Short version of A-IADL for leisure activities and IADLs in MCI/mild dementia.	Yes	No	30 items from seven categories. Computer scored against normative distribution	Computerized administration. Psychometric properties of A-IADL well studied. Available to professionals for clinical and non-profit use with registration at: https://www.alzheimercentrum.nl/professionals/amsterdam-iadl/

Abbreviations: AD, Alzheimer's disease; ADL, activities of daily living; ADRD, Alzheimer's disease related disorders; A-IADL-SV, Amsterdam IADL-short version; BADL, basic activities of daily living; CDR, Clinical Dementia Rating; DAD, Disability Assessment for Dementia Scale; DAD-6, six-item version of the DAD scale; FAQ, Functional Activities Questionnaire; FAST, Functional Assessment Staging Scale; IADL, instrumental activities of daily living; MCI, mild cognitive impairment.

The clinician needs to be aware of any alterations in sensory or motor function (especially vision, hearing, gait, and balance) to fully interpret symptoms of cognitive or behavioral change. Hearing loss (presbycusis), a known and potentially reversible dementia risk factor,[95] is very common in the elderly[96] as is visual loss (presbyopia).[97] Some components of hearing or visual dysfunction related to primary sensory inputs (as opposed to processing and integration of auditory and visual signals in brain networks) are also amenable to treatments that can mitigate cognitive or behavioral symptoms, maintain or improve daily activities, and reduce safety risks.

Gait and balance problems take on added importance in the evaluation and management of people who are cognitively impaired. Fall risk may be substantially increased when sensorimotor, gait, or balance problems co-occur with cognitive or behavioral impairments in insight, judgment, impulse control, attention, memory, psychomotor processing, and visuospatial awareness. Gait and balance impairment can point to a group of disorders in which impaired cognition, behavior, and impaired motor function co-occur, the most common being a Parkinson's spectrum disorder (manifesting as Dementia with Lewy Bodies [DLB] or Parkinson's disease dementia), vascular cognitive impairment or dementia, or one of the diseases linked to frontotemporal lobar degeneration such as progressive supranuclear palsy or corticobasal degeneration. In some patients, a gait disorder can be the most prominent symptom. Gait and balance disorders also have predictive utility of future risk for developing dementia.[98] Distal polysensory neuropathy, particularly in the feet/legs, is common in older individuals, can be idiopathic or due to long-term sequelae of chronic microvascular insufficiency, and is a fall risk that may be treated (e.g., in vitamin B12 deficiency) or mitigated (e.g., by use of assistive device, night light, shower grab bars, and eliminating trip hazards). Some sensorimotor impairments in persons with cognitive and behavioral syndromes are amenable to early intervention and sustained treatments and exercises (e.g., formal physical therapy assessment and treatment of gait and balance, home occupational therapy, and safety assessment). Improved balance or limb motor function can benefit daily functions and reduce safety risks.[99]

1.6 | History of sleep disturbance

In an evaluation of a patient with cognitive or behavioral symptoms, a clinician should always ask questions about sleep. Instruments useful for this purpose include the Mayo Sleep Questionnaire[100] or the Scales for Outcomes in Parkinson's Disease (SCOPA).[101] Sleep-related symptoms may be hallmarks of certain neurodegenerative diseases causing dementia, or sleep disorders may adversely impact overall function in any individual, particularly those with MCI or dementia; addressing sleep problems through lifestyle interventions improves general health.[95] Rapid eye movement (REM) sleep behavior disorder—with loss of REM-associated atonia resulting in acting out of dreams, often violently—has a strong association with LBD.[102] Symptoms of REM sleep behavior disorders are even more likely to be under-reported by informants and, almost never, by patients.[103] REM sleep behavioral disturbances may precede by many years what ultimately evolves to become DLB or Parkinson's-related dementia.[104] In cognitively unimpaired persons, reduced slow-wave sleep activity and low sleep efficiency are both associated with accelerated rate of cortical amyloid beta plaque deposition, and hence accumulation of AD-related neuropathological change.[105]

Sleep disorders have multiple relationships with cognitive and behavioral syndromes. Obstructive sleep apnea (OSA) is deleterious to optimal brain function and health. It is common in MCI[106] and can exacerbate impairments in cognition, mood/behavior, and/or function. Treatment of OSA may reverse cognitive and behavioral decline in some patients.[107]

1.7 | Examination

Primary care clinicians hold a key relationship with their patients who often trust them for information, guidance, endorsement, recommendations, and referrals.[108] Primary care providers are also often in the best position to detect early signs on examination of a cognitive–behavioral syndrome as it is developing given their longitudinal relationship with the patient, even if mental status was not previously formally assessed. It may be obvious to a primary care clinician that a patient's cognition, mood, or behavior is clearly different relative to their baseline, prompting a formal mental status examination. Or, concerns raised in the history or by information provided from an informant may identify the need for a mental status examination. A first-tier mental status examination of cognitive ability, mood, and behavior may be efficiently completed within a problem-focused primary care visit. The goal of such an assessment is to detect, with acceptable sensitivity, the presence of potentially clinically significant lower-than-expected or impaired cognitive performance, or abnormal mood or behavior. We recommend that a mental status examination include the use of a validated brief cognitive assessment test instrument(s) (Table 4).

In addition, the primary care clinician should perform and document a dementia-focused elemental neurologic examination. This neurologic exam should aim to efficiently screen for potential abnormalities of cranial nerve function, somatosensory or motor function, or postural/gait abnormalities (video tutorial demonstrations of the neurological examination can be found online[127,128]). Abnormalities identified on the neurologic exam not only need to be considered in the diagnostic formulation,[129] but also may raise questions about potential safety risks. If the primary care clinician is unsure about the interpretation or implication of abnormalities on the neurologic exam, referral to a specialist is warranted.

There is no "one size fits all" brief, validated cognitive test to assess a patient for cognitive impairment in the primary care setting. Multiple tests have been validated against a gold standard of comprehensive clinical and neuropsychological evaluation and are available for the brief evaluation of cognitive performance in the primary care setting. Each test has its unique profile of sensitivity, specificity, strengths, limitations, and considerations regarding effort, efficiency, copyright, and training/certification. For routine evaluation in primary care, several

TABLE 4 Validated mental status test instruments.

Name	Time (minutes)	Considerations
MoCA[13]	10–15	Widely available in multiple versions and languages, well suited for detection of MCI; tracks progression through mild to moderate dementia. Interpret with caution in individuals with low education. Range 0–30 (max performance). MoCA domain index scores (e.g., MIS) are easily calculated and helpful to delineate pattern of performance on cognitive domains. MoCA is freely available. Training/certification at mocatest.org MoCA variants adapted for telemedicine available (see Box 1)
MMSE[109,110]	7–10	Widely known and well studied; more suited for detection of dementia; lower sensitivity for detection of MCI and tracks progression through severe dementia. Range 0–30 (max performance). Proprietary—not free for clinical use. MMSE-like variants have been adapted for telemedicine (see Box 1)
Mini-Cog[111]	2–4	Combines three-time word list learning and recall with clock drawing test; provides rapid screen—more suitable for detection of dementia than MCI. Is available as part of Alzheimer's Association Cognitive Assessment Toolkit along with GPCOG, Clock Drawing Test, and Memory Impairment Screen at: https://www.alz.org/media/documents/cognitive-assessment-toolkit.pdf
GPCOG[112]	Patient 2–5 informant 1–3	Widely used outside United States in general practitioner setting; more suited for detection of dementia; lower sensitivity MCI detection. Includes a clock drawing test with range of 0–2. Range of 0–9 on patient exam. Informant component (when complaint is informant-based or score on patient exam is < 9) has a range of 0–4. https://www.alz.org/media/documents/cognitive-assessment-toolkit.pdf
SLUMS [113]	7–10	Developed and mostly used in VA population; suited to detection of MCI and dementia; tracks progression through moderate stages dementia. Range 0–30 (max performance). Available at: http://aging.slu.edu/pdfsurveys/mentalstatus.pdf
M-ACE [114]	5–8	A short version of items from the ACE-III (see below) that includes temporal orientation (0–4 points); learning of a name and address (0–7 points) with delayed recall (0–7 points) after distractor tasks of animal naming in 60 s (0–7 points) and a clock drawing test (0–5 points); range 0–30 (max performance). Better sensitivity for dementia than MMSE at all cut-offs due to less ceiling effect.
Blessed OMC Test (OMCT, BOMC), aka Short Blessed Test (SBT; 6-Item Cognitive Impairment Test 6-CIT)[115]	5–7	Short version of BDS-IMC; more suited to detection of amnestic dementia; verbal only (no writing/drawing); heavily weighted toward memory and information; does not assess visuospatial and executive functions and can be administered via telemedicine. Requires weighting of scores. Range from 0 to 28 (original version counted errors—28 was max for errors). Available at: http://regionstrauma.org/blogs/sbt.pdf and page 3 of: https://www.mirecc.va.gov/visn4/BHL/docs/Vol_5_Clinician_Resources.pdf
MIS[116]	4–5	A four-item delayed free- and cued-recall test of memory; uses controlled learning to assess remembering of four written items; range 0–8 (2 x items freely recalled + items with cued recall). Available at: https://www.alz.org/media/Documents/memory-impairment-screening-mis.pdf
AMTS[117]	3-5	A 10-item scale that assesses orientation, registration and recall, and concentration. Does not assess visuospatial function. Scores of 6 or below, from a maximum score of 10, suggest potential dementia level performance. May not have high sensitivity for detection of MCI, particularly non-amnestic MCI.
BIMS[118]	2–3	Cognitive screener used in nursing homes as part of Minimal Data Set 3.0. Consists of repetition of three words, temporal orientation to month, year and day; and recall of three words. BIMS scores range from 0 to 15 (cognitively intact 13–15; moderate impairment 8–12; severe impairment 0–7). Available at: https://www.aanac.org/docs/mds-3.0-rai-users-manual/11118_mds_3-0_chapter_3_-_section_c_v1-12.pdf?sfvrsn=6
Clock Drawing Test[119]	1–2	Quick screen of aspects of visuospatial cognition, conceptualization, and executive function (planning/organization); qualitative assessment can inform regarding errors in conceptual design (including meaning of a clock), stimulus boundedness, perseveration, visual spatial relations, planning, and graphomotoric function. Several variations and scoring systems possible—with max scores often ranging from 3 to 10 (on MoCA performance range is 0–3); avoid using in isolation. https://www.alz.org/media/documents/cognitive-assessment-toolkit.pdf

(Continues)

TABLE 4 (Continued)

Name	Time (minutes)	Considerations
T&C[120]	2–4	Two tasks to determine "dementia" level impairment: tell the time presented on a clock face, and make $1 when provided by 3 quarters, 7 dimes, and 7 nickels; avoid using in isolation
7MS[121]	7–12	Developed and suited for detection of AD/dementia; components test memory (enhanced free and cued recall), temporal orientation, semantic (animal category) verbal fluency and a 7-point clock drawing test, administration and scoring may be better suited for specialty setting
STMS[122]	10–15	Robust test for assessing several domains to detect and track MCI and dementia; validated in primary care, administration and scoring may be better suited for specialty setting. More sensitive than MMSE to distinguish normal cognition from prevalent MCI; superior to MMSE in detecting subtle cognitive performance deficits in individuals with normal cognition who later developed incident MCI or AD dementia. Score range 0–37 (max performance). Available at: https://www.ouhsc.edu/age/Brief_Cog_Screen/documents/STMS.pdf
Blessed Dementia Scale Information-Memory-Concentration Test (BDS-IMC; BIMC)[123]	10–15	Well-validated for AD neuropathology and detecting and tracking AD dementia progression from mild through very severe stages. May not have high sensitivity to detect non-amnestic MCI. Verbal tests (no writing/copying) with emphasis on memory and information (limited executive function and no visuospatial component) and can be administered via telemedicine. Score range 0–37 errors (37 is max errors; higher score denotes worse performance)
CAMCOG[124]	20–25	Suited for specialty settings; provides cognitive domain scores through eight major subscales (orientation, language, memory, attention, praxis, calculation, abstract thinking, perception); is part of CAMDEX interview; score range 0–106 (max performance)
ACE-III[125]	20–30	Suited for specialty settings; provides multiple cognitive domains including specific scores for attention, memory, fluency, language, and visuospatial; useful for delineating cognitive-behavioral syndrome and differential diagnosis. Score range 0–100 (max performance)
FAB[126]	10	Suited for specialty settings; provides a structured examination of frontal systems function by assessing conceptualization, mental flexibility, motor programing, sensitivity to interference, inhibitory control, and environmental autonomy. Score range 0–18 (max performance)

Abbreviations: 7MS, 7-minute screen; ACE, Addenbrooke's Cognitive Exam; AD, Alzheimer's disease; AMTS, Abbreviated Mental Test Score; BIMS, Brief Interview for Mental Status; CAMCOG, Cambridge Cognitive Examination; CAMDEX, Cambridge Mental Disorders of the Elderly Examination; FAB, Frontal Assessment Battery; GPCOG, General Practitioner Assessment of Cognition; M-ACE, Mini Addenbrooke's Cognitive Exam; MCI, mild cognitive impairment; MIS, Memory Index Score; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; SLUMS, St. Louis University Mental Status; STMS, Short Test of Mental Status; T&C, Time and Change Test; VA, Veterans Administration.

instruments have shown acceptable performance characteristics to assist with the detection of dementia or MCI (Tables 4 and 5). When a clinician uses a brief validated cognitive test, it enables her/him to interpret scores to determine the likelihood of clinically significant impairment and may provide a gross estimate of the severity of cognitive impairment. Depending upon clinician proficiency with the assessment of patients with dementia, practice setting, time available for testing, and patient characteristics (e.g., level of education and occupational attainment, language and cultural considerations), the primary care clinician should choose a test(s) best suited to play this important role in the diagnostic evaluation. In some cases, a patient's cognitive test performance will be congruent with the history, and the clinician will find it straightforward to integrate this information with the history and risk profile to develop the diagnostic formulation. In other cases, cognitive test performance may be inconsistent with the history and clinician's pre-test level of concern. A brief validated cognitive test should not be used in isolation, particularly with binary cut-off scores, to adjudicate the presence or absence of MCI or dementia or a specific cognitive–behavioral syndrome. For patients in whom the history and clinician's pre-test concern are incongruent with the patient's performance on a brief cognitive test, biopsychosocial and other factors should be considered and a referral to a neuropsychologist or other specialist should be considered.[19]

The Mini-Mental State Examination (MMSE)[109,110] is the most widely known and best-studied brief test of cognition that usually takes < 10 minutes to administer.[88–90,130,131] However, it currently has copyright restrictions on its use, and alternative tools are available for use in medical practice that have comparable (for dementia) or better (for MCI—e.g., MoCA, see below) diagnostic accuracy than the MMSE.

The Mini-Cog is a very quick (2–3 minutes) test that contains two items: a measure of short-term memory (short-delay recall of three words), and a measure of visuospatial ability and executive functions

TABLE 5 Comparison of selected brief cognitive tests to detect cognitive impairment or dementia.

Name	MoCA	MMSE	Mini-Cog	SLUMS	M-ACE	GPCOG
Time to administer (minutes)	10–15	7–10	2—4	7–10	6–9	2–5 patients 1–3 informant
Cutoff for potential cognitive impairment	< 26/30 (1 point added to raw score if ≤ 12 years of education	< 26/30	≤ 3/5	< 27/30 for ≥ 12 years of education < 25/30 for ≤ 12 years of education	Two suggested: < 26/30 has 92% positive predictive value (PPV); < 22 has 100% PPV for dementia (62% sensitivity, 100% specificity)	< 5 patient Or < 8 patient and < 4 informants
Sensitivity for cognitive impairment	90%	81%	76%	96%	80%–85%	85%
Specificity for cognitive impairment	87%	82%	89%	61%	85%–87%	86%
Cognitive domains assessed						
Complex attention	✓	✓		✓		
Executive function	✓		✓	✓	✓	✓
Learning and memory	✓	✓	✓	✓	✓	✓
Language	✓	✓		✓	✓	
Visual construction	✓	✓	✓	✓	✓	✓
Orientation	✓	✓		✓	✓	✓
Available in multiple languages?	Yes	No	Yes	No	No	Yes
Other considerations	● Index scores can be calculated to better inform domain-specific performance ● Mixed findings in people with low education	● Well-known among clinicians ● Purchase required ● Limited evidence for sensitivity to detect mild changes	● Simple scoring algorithm ● Limited evidence for sensitivity to detect mild changes	● Evidence for sensitivity to detect mild changes ● Largely studied in veteran populations	● Provides broad range for learning and memory performance (14 points) ● Limited direct assessment of language—only verbal fluency for semantic animal category tested	● Validated in primary care settings ● Limited evidence for sensitivity to detect mild changes

Abbreviations: GPCOG, General Practitioner Assessment of Cognition; M-ACE, Mini Addenbrooke's Cognitive Exam; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; SLUMS, St. Louis University Mental Status.

(Clock Drawing Test).[111] It has acceptable diagnostic accuracy for detection of cognitive impairment and has been evaluated in four large systematic reviews.[88–90,131] It is, however, validated as a screening test (not a diagnostic test), and, like the MMSE, may have low sensitivity to detect MCI in more intellectually capable individuals.

The MoCA is a 20-item test that assesses multiple cognitive domains (orientation, memory, language, attention, visuospatial, and executive functions) and usually takes 12 to 15 minutes to administer.[13] The diagnostic accuracy of the MoCA for identifying persons with cognitive impairment or dementia has been studied in systematic reviews with up to 34 studies[89,90,131,132] and appears to be more accurate than the MMSE to detect MCI.[132] While the MoCA can be good at detecting MCI in most individuals with average or above levels of education, performance on the MoCA can be highly sensitive to low levels of education; the adapted MoCA–B provides enhanced diagnostic accuracy for patients with < 4 years of education. Like the MMSE, the MoCA has been translated and validated in many languages, enhancing the diagnostic accuracy in diverse primary care populations. Training and certification on the use of the MoCA is available online. Finally, MoCA domain-specific index scores for performance on memory (e.g., Memory Index Score [MIS]), attention, orientation, executive function, language, and visuospatial cognition can be easily calculated from MoCA item scores.[133] The pattern of performance on MoCA index scores can be helpful to inform regarding the cognitive–behavioral syndrome, and hence probabilistically regarding potential etiology and progression of cognitive–functional status.[134–136]

The General Practitioner Assessment of Cognition (GPCOG) is a 15-item test that assesses multiple cognitive domains (orientation, memory, language, visuospatial ability, executive function, and other daily living functions) has been evaluated in three large systematic reviews with high sensitivity and specificity.[89,90,131] This tool is unique in that it combines both measures of cognition and function.

Several other tests with very short administration times (1–2 minutes) that provide flexibility and convenience for primary. care providers include the Clock Drawing Test (Shuman and Clock Drawing Test—Sunderland), the Memory Impairment Screen, the Abbreviated Mental Test (AMT), and the Verbal Fluency Test.[89,90,131] However, due to the very short and focused nature of such instruments, they may provide limited sensitivity to detect broader cognitive impairments in the domains not assessed by these tests.

See Table 5 for summary comparisons, including diagnostic accuracy, of commonly used brief validated cognitive tests and the NIA and Alzheimer's Association websites for links to assessments and other helpful diagnostic tools and websites. Several references provide further information about the relative strengths and limitations of commonly used cognitive tests as well as pragmatics and approaches regarding their use in primary care settings.[3,4,137,138] This reference provides a systematic review of cognitive screening instruments.[139] For a review of single-domain cognitive tests for use in the neurobehavioral status exam that are suitable for specialty and dementia subspecialist settings see the American Academy of Neurology Behavioral Neurology Section Workgroup Report on Clinical Cognitive Testing.[140] The use of telehealth for the assessment of patients with symptoms of cognitive decline is discussed in Box 1.

2 | CONCLUSIONS

The cornerstone of the diagnostic assessment of a patient with symptoms concerning AD or ADRD is the history and examination. Although advances in molecular biomarkers of brain diseases leading to cognitive impairment will likely enable their detection in some patients at an asymptomatic stage, the ability of proficient clinicians to recognize and diagnose patients in the early symptomatic stages of these illnesses is critical to optimize early management and hopefully minimize the adverse impact of these diseases on daily function and safety. Although it is common for a history to be taken and an examination to be performed without the use of specific validated instruments, evidence indicates and the DETeCD-ADRD workgroup strongly believes that the use of such instruments will lead to better outcomes. Instruments to assess symptoms in daily life and their impact on function can be given to patients and informants prior to an office visit and can serve as a mechanism for structuring the history and efficiently identifying areas for focused clinical interviewing while also providing a list of pertinent negatives. A brief neurologic exam tailored to the patient is also important, as is a mental status exam augmented with a validated cognitive assessment instrument. The score on the test should not be interpreted in isolation, but should be integrated with information from the HPI, the patient's demographic background and psychosocial history, family history and other information relevant to the risk profile, medical history, medications, and other relevant information. For proficient clinicians, the synthesis of this information should lead to a diagnostic formulation of the patient's cognitive functional status and cognitive-behavioral syndrome. In some cases, neuropsychological assessment or additional consultation(s) may be required to develop or further refine these first two steps of the diagnostic formulation.

BOX 1: Pragmatic Adoption of the DETeCD-ADRD CPG in the Context of Remote Assessment of Cognitive Impairment and Dementia

Telemedicine has been emerging over the past decade for a variety of purposes, particularly to enable better access to medical specialty services. With the pandemic of 2020, the field exploded. Many of the core elements and recommendations of this clinical practice guideline can be adapted pragmatically for telemedicine. Core elements 1-4 and 7 are readily adaptable to telemedicine formats as they involve patient-centered discussions of processes and goals; interview-based history taking, review of systems, questionnaires and assessments; and communication of findings and development of a shared plan of care (Recommendations 1-5, 10-11). There is also evidence to support that cognitive-behavioral examination including administration of brief mental status test instruments can also be pragmatically adapted to the telemedicine format[141] and so can neuropsychological evaluation by a skilled neuropsychologist (Recommendation 14).[142] Some elements of the physical and neurologic examination that require the direct laying on of hands are not possible in a remote format (e.g., elements of Core 5 and Recommendations 6, 13) and the vast majority of Tier 1-4 laboratory tests and studies (Recommendations 8-9; 15-19) would require a visit to a laboratory, imaging facility, or other medical facility. Nevertheless, we believe it is possible to adapt much of the material in these guidelines to telemedicine, enabling the detection of impaired Cognitive Functional Status and the characterization of the Cognitive-Behavioral Syndrome. By accomplishing these goals, it may be possible in many patients to begin to develop the differential diagnosis of potential etiology(-ies) and guide next steps in evaluation, disclosure and care.

The instruments in Tables 1-5 are readily adaptable to telemedicine to assist in characterization of cognitive symptoms, neuropsychiatric symptoms, behaviors and mood, functional impairment in activities of daily living, and staging of dementia. Home-based telemedicine assessment of key domains of cognition, daily function and behavior in individuals older than 75 years of age is feasible and can detect and track cognitive impairments[142]; these have included assessment of cognitive performance with brief validated mental status instruments designed for telephone administration such as the TICS (Telephone Interview for Cognitive Status),[143] as well as neuropsychological tests of memory, attention/concentration, executive functions and processing speed.[142,144] Different variants of the TICS have been validated for telephone administration and cut-off scores and correspondence to MMSE scores have been reported.[145]

Several of the standardized mental status test instruments that have been adapted to telemedicine do not have motoric or visuospatial components and only require verbal responses (e.g. SBT, BDS-IMC) thus facilitating their easy administration by telephone or video. Other common instruments have variants that have been adapted for telephone or video administration, including the MoCA and variants of the MMSE.

Various options exist for telemedicine administration of the MoCA (see https://www.mocatest.org/remote-moca-testing/), with the caveat that they require further validation for specific cut-offs and potential age- and education-adjustments. These include the "Telephone MoCA" which, similarly to the MoCA-Blind/Visually Impaired (MoCA-B),[146] does not administer the first 4 items of the full MoCA (mini Trails-B; 3-D figure copy; clock test, naming of 3 animal drawings) that have a visual or motoric component, and that account for 8 points; hence the MoCA-B has a range of 0-22. An approximate cut off score of 18 (that converts proportionally to a score of 25.5 on the 30-point MoCA, which is approximately 26 and the cut-off of possible impairment) has been suggested as possibility indicating cognitive impairment, but this requires further validation. Directions for adaptation and administration of a full MoCA-variant via audio-videoconference (thus ranging from 0-30), that includes adapted administration of the first 4 items, can also be found at https://www.mocatest.org/remote-moca-testing/. For example, adaptions include for the mini Trails B to be presented to the patient on video and to ask the patient to "please tell me where the arrow should go to next with respect to the pattern I am showing you?"; and for orientation to place and city, to ask the patient "where is the clinic/institution I am calling you from?" and "what is the city in which our clinic/institution is located?". For such MoCA-variants, preliminary evidence supports acceptable test-retest and inter-rater reliability and patient satisfaction of in-person versus audiovideo administration.[147,148] Variations of MMSE-like tests have also been studied and validated for telephone administration, and include 22-point (e.g. ALFI-MMSE,[149] MMSET[150]) and 26-point variants (TMMSE[151]); these often omit or adapt questions such as following a 3-step command, reading and repeating a sentence, reading and obeying a command, writing a sentence, and copying intersecting figures, and may shorten the naming task to one item (instead of two), by asking the patient to "name the thing you are speaking into as you talk to me" (the telephone).

While best clinical practice guidelines for tele-neuropsychological assessments will need to be developed, there is already a substantial evidence-base to support the reliability and validity of neuropsychological evaluation of patients by experienced professionals utilizing tele-neuropsychological (especially via video conference) assessment.[142,144,152–155] The administration of verbally-mediated tasks using existing norms is supported, and pragmatic use of visually dependent tasks can be adapted.[144] Gaps to address include development of standardized methods for the presentation of visual stimuli, and development and incorporation of complex tasks often used to assess processing speed, complex attention, and those that rely on motor and visual abilities.[144]

A strong and growing evidence base demonstrates that telemedicine does not impede and in many ways can facilitate successful clinical, cognitive and neuropsychological evaluation of patients with cognitive impairments. While older individuals and those with cognitive

impairments can have unique challenges with remote testing, including access and use of video technology, yet these can be surmountable with dedicated effort and resources. The principal benefits of telemedicine can include improved access to care, patient satisfaction, convenience, a lower burden on working family members/informants to participate, mitigation of exposure risks for vulnerable individuals, and potential cost savings.[142,144,155] We will undoubtedly see further guidance on methods for remote cognitive assessment and further evidence regarding validity against in-person administration, as well as practical utility.

If a patient has MCI or dementia, an evaluation should be done to determine the likely etiology, if possible, as discussed extensively in the companion articles.[19,156] These diagnostic elements set prior probabilities on the differential diagnosis of likely etiology (-ies), which informs clinical decision making regarding Tier 1 to 4 tests and other assessments in the evaluation process. See the primary care companion article for discussion of structural neuroimaging and cognitive lab panel blood tests.[19] In some cases, the steps in this process may be relatively straightforward, and in others they may be quite complex. See the specialty care companion article for discussion of specialized functional and molecular neuroimaging and for fluid molecular biomarkers.[156] Ultimately, the evaluation process should lead to a diagnostic formulation that is communicated clearly and compassionately to the patient and care partner, along with a discussion of management and prognosis.

AUTHOR CONTRIBUTIONS

Concept and design: All authors. Acquisition; analysis; or interpretation of data: All authors. *Drafting of the manuscript*: Atri, Dickerson. *Critical revision of the manuscript for important intellectual content*: All authors. *Administrative; technical; or material support*: Atri, Dickerson, Carrillo. *Supervision*: Atri, Dickerson, Carrillo.

ACKNOWLEDGMENTS

We are grateful to our colleagues who served as external peer reviewers; to Roger Chou, MD, Jesse Wagner, MA, Tracy Dana, MLS, Miranda Pappas, MA, Ian Blazina, MPH, Lucy Stillman, BS of the Pacific Northwest Evidence-based Practice Center, Oregon Health & Science University who conducted the evidence review and synthesis; to Alzheimer's Association staff Jim Hendrix, PhD (former), April Ross, PhD (former), Christopher Weber, PhD; and to Avalere staff Sheila Fifer, Judit Illes (former), Courtney Ramus, Michelle Bruno. No compensation outside of regular salary was received by any named contributor. The DETeCD-ADRD Guideline report was funded by the Alzheimer's Association. Role of the Funder/Sponsor: The Alzheimer's Association staff agreed with the co-chairs about the need for this guideline, contracted with Avalere and the Pacific Northwest Evidence-based Practice Center, worked with the co-chairs to select the expert panel members, and provided administrative support and oversight. The expert panel designed the approach to review the evidence; review and interpretation of the data; and preparation, review, and approval of the guideline and the comprehensive report.

CONFLICT OF INTEREST STATEMENT

Dickerson: consulting for Acadia, Alector, Arkuda, Biogen, Eisai, Med Learning Group, Quanterix; DSMB for Lilly, Merck; royalties from Cambridge University Press, Elsevier, Oxford University Press, Up To Date. Atri: consulting for Acadia, AriBio, AZ Therapies, Biogen, Eisai, JOMDD, Lundbeck, Life Molecular Imaging, Merck, ONO, Prothena, Roche/Genentech, Novo Nordisk, Qynapse, Vaxxinity; royalties from Oxford University Press. Clevenger: none. Karlawish: DSMB for Linus Health. Knopman: DSMB for DIAN TU. Lin: consulting for Lilly. Norman: none. Onyike: consulting for Acadia Pharmaceuticals, Reata Pharmaceuticals, Otsuka Pharmaceutical, Eisai Pharmaceutical, Lykos Therapeutics, Zevra Therapeutics. Sano: consulting for Eisai, NovoNordisk, Otsuka Lundbeck. Scanland: employee of Dementia Connection, LLC, consulting for Axsome, BioXcel, Eisai, Genentech, Lundbeck, Otsuka. Carrillo: Employee of Alzheimer's Association. Author disclosures are available in the supporting information.

DATA AVAILABILITY STATEMENT

Drs. Atri and Dickerson had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

REFERENCES

1. Cordell CB, Borson S, Boustani M, et al. Alzheimer's association recommendations for operationalizing the detection of cognitive impairment during the Medicare annual wellness visit in a primary care setting. *Alzheimers Dement*. 2013;9:141-150.
2. Jack CR Jr, Bennett DA, Blennow K, et al. NIA-AA research framework: toward a biological definition of Alzheimer's disease. *Alzheimers Dement*. 2018;14:535-562.
3. Patnode CD, Perdue LA, Rossom RC, et al. *U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. Screening for Cognitive Impairment in Older Adults: An Evidence Update for the US Preventive Services Task Force*. Agency for Healthcare Research and Quality (US); 2020
4. Patnode CD, Perdue LA, Rossom RC, et al. Screening for cognitive impairment in older adults. *JAMA*. 2020;323(8):764-785.
5. Petersen RC, Yaffe K. Issues and questions surrounding screening for cognitive impairment in older patients. *JAMA*. 2020;323(8):722-247.
6. Foster NL, Bondi MW, Das R, et al. Quality improvement in neurology: Mild cognitive impairment quality measurement set. *Neurology*. 2019;93:705-713.
7. Jack CR Jr, Albert MS, Knopman DS, et al. Introduction to the recommendations from the national institute on aging-Alzheimer's association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7:257-262.
8. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the national institute on aging-Alzheimer's association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. 2011;7:270-279.
9. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders: DSM-5*.: American Psychiatric Association; 2013
10. Petersen RC, Lopez O, Armstrong MJ, et al. Practice guideline update summary: mild cognitive impairment: report of the guideline development, dissemination, and implementation subcommittee of the American academy of neurology. *Neurology*. 2018;90:126-135.

11. Dubois B, Feldman HH, Jacova C, et al. Advancing research diagnostic criteria for Alzheimer's disease: the IWG-2 criteria. *Lancet Neurol*. 2014;13:614-629.
12. Dubois B, Hampel H, Feldman HH, et al. Preclinical Alzheimer's disease: definition, natural history, and diagnostic criteria. *Alzheimers Dement*. 2016;12:292-323.
13. Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal cognitive assessment (MoCA): a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53:695-699.
14. Molinuevo JL, Rabin LA, Amariglio R, et al. Implementation of subjective cognitive decline criteria in research studies. *Alzheimers Dement*. 2017;13:296-311.
15. Mortby ME, Lyketsos CG, Geda YE, Ismail Z. Special issue on mild behavioral impairment and non-cognitive prodromes to dementia. *Int Psychogeriatr*. 2018;30:167-169.
16. Mallo SC, Ismail Z, Pereiro AX, et al. Assessing mild behavioral impairment with the mild behavioral impairment-checklist in people with mild cognitive impairment. *J Alzheimers Dis*. 2018;66:83-95.
17. Ismail Z, Agüera-Ortiz L, Brodaty H, et al. The mild behavioral impairment checklist (MBI-C): a rating scale for neuropsychiatric symptoms in pre-dementia populations. *J Alzheimers Dis*. 2017;56:929-938.
18. Ismail Z, Smith EE, Geda Y, et al. Neuropsychiatric symptoms as early manifestations of emergent dementia: provisional diagnostic criteria for mild behavioral impairment. *Alzheimers Dement*. 2016;12:195-202.
19. Atri A, et al. The Alzheimer's Association clinical practice guideline for the diagnostic evaluation, testing, counseling and disclosure of suspected Alzheimer's disease and related disorders (DETeCD-ADRD): Executive summary of recommendations for primary care. *Alzheimer's Dement*. in press. doi:10.1002/alz.14333
20. Carr DB, Gray S, Baty J, Morris JC. The value of informant versus individual's complaints of memory impairment in early dementia. *Neurology*. 2000;55:1724-1726.
21. Gifford KA, Liu D, Hohman TJ, et al. A mutual self- and informant-report of cognitive complaint correlates with neuropathological outcomes in mild cognitive impairment. *PLoS One*. 2015;10:e0141831
22. Rabin LA, Wang C, Katz MJ, Derby CA, Buschke H, Lipton RB. Predicting Alzheimer's disease: neuropsychological tests, self-reports, and informant reports of cognitive difficulties. *J Am Geriatr Soc*. 2012;60:1128-1134.
23. Rueda AD, Lau KM, Saito N, et al. Self-rated and informant-rated everyday function in comparison to objective markers of Alzheimer's disease. *Alzheimers Dementia*. 2015;11:1080-1089.
24. Silva MR, Moser D, Pfluger M, et al. Self-reported and informant-reported memory functioning and awareness in patients with mild cognitive impairment and Alzheimer s disease. *Neuropsychiatr*. 2016;30:103-112.
25. Tierney MC, Herrmann N, Geslani DM, Szalai JP. Contribution of informant and patient ratings to the accuracy of the mini-mental state examination in predicting probable Alzheimer's disease. *J Am Geriatr Soc*. 2003;51:813-818.
26. Isella V, Villa L, Russo A, Regazzoni R, Ferrarese C, Appollonio IM. Discriminative and predictive power of an informant report in mild cognitive impairment. *J Neurol Neurosurg Psychiatry*. 2006;77:166-171.
27. Mackinnon A, Khalilian A, Jorm AF, Korten AE, Christensen H, Mulligan R. Improving screening accuracy for dementia in a community sample by augmenting cognitive testing with informant report. *J Clin Epidemiol*. 2003;56:358-366.
28. Mackinnon A, Mulligan R. Combining cognitive testing and informant report to increase accuracy in screening for dementia. *Am J Psychiatry*. 1998;155:1529-1535.
29. Jorm AF. A short form of the informant questionnaire on cognitive decline in the elderly (IQCODE): development and cross-validation. *Psychol Med*. 1994;24:145-153.
30. Jorm AF. The informant questionnaire on cognitive decline in the elderly (IQCODE): a review. *Int Psychogeriatr*. 2004;16:275-293.
31. Jorm AF, Jacomb PA. The informant questionnaire on cognitive decline in the elderly (IQCODE): socio-demographic correlates, reliability, validity and some norms. *Psychol Med*. 1989;19:1015-1022.
32. Galvin JE, Roe CM, Powlishta KK, et al. The AD8: a brief informant interview to detect dementia. *Neurology*. 2005;65:559-564.
33. Galvin JE. The quick dementia rating system (QDRS): a rapid dementia staging tool. *Alzheimers Dement*. 2015;1:249-259.
34. Malek-Ahmadi M, Sabbagh MN. Development and validation of the Alzheimer's questionnaire (AQ). *J Nat Sci*. 2015;1:e104
35. Sabbagh MN, Malek-Ahmadi M, Kataria R, et al. The Alzheimer's questionnaire: a proof of concept study for a new informant-based dementia assessment. *J Alzheimer's Dis*. 2010;22:1015-1021.
36. Farias ST, Mungas D, Reed BR, et al. The measurement of everyday cognition (ECog): scale development and psychometric properties. *Neuropsychology*. 2008;22:531-544.
37. Tomaszewski Farias S, Mungas D, Harvey DJ, Simmons A, Reed BR, Decarli C. The measurement of everyday cognition: development and validation of a short form of the everyday cognition scales. *Alzheimers Dement*. 2011;7:593-601.
38. Walsh SP, Raman R, Jones KB, Aisen PS, Alzheimer's Disease Cooperative Study G. ADCS prevention instrument project: the mail-in cognitive function screening instrument (MCFSI). *Alzheimer Dis Assoc Disord*. 2006;20:S170-S178.
39. Li C, Neugroschl J, Luo X, et al. The utility of the cognitive function instrument (CFI) to detect cognitive decline in non-demented older adults. *J Alzheimers Dis*. 2017;60:427-437.
40. Rattanabannakit C, Risacher SL, Gao S, et al. The cognitive change index as a measure of self and informant perception of cognitive decline: relation to neuropsychological tests. *J Alzheimers Dis*. 2016;51:1145-1155.
41. Wedderburn C, Wear H, Brown J, et al. The utility of the Cambridge behavioural inventory in neurodegenerative disease. *J Neurol Neurosurg Psychiatry*. 2007;79(5):500-503.
42. Nagahama Y, Okina T, Suzuki N, Matsuda M. The Cambridge behavioral inventory: validation and application in a memory clinic. *J Geriatr Psychiatry Neurol*. 2006;19:220-225.
43. Wear HJ, Wedderburn CJ, Mioshi E, et al. The Cambridge behavioural inventory revised. *Dement Neuropsychol*. 2008;2:102-107.
44. Okereke OI, Copeland M, Hyman BT, Wanggaard T, Albert MS, Blacker D. The structured interview & scoring tool-Massachusetts Alzheimer's disease research center (SIST-M): development, reliability, and cross-sectional validation of a brief structured clinical dementia rating interview. *Arch Neurol*. 2011;68:343-350.
45. Okereke OI, Pantoja-Galicia N, Copeland M, et al. The SIST-M: predictive validity of a brief structured clinical dementia rating interview. *Alzheimer Dis Assoc Disord*. 2012;26:225-231.
46. Vik-Mo AO, Giil LM, Ballard C, Aarsland D. Course of neuropsychiatric symptoms in dementia: 5-year longitudinal study. *Int J Geriatr Psychiatry*. 2018;33:1361-1369.
47. Vik-Mo AO, Giil LM, Borda MG, Ballard C, Aarsland D. The individual course of neuropsychiatric symptoms in people with Alzheimer's and Lewy body dementia: 12-year longitudinal cohort study. *Br J Psychiatry*. 2020;216(1).
48. Cummings J, Pinto LC, Cruz M, et al. Criteria for psychosis in major and mild neurocognitive disorders: international psychogeriatric association (IPA) consensus clinical and research definition. *Am J Geriatr Psychiatry*. 2020;28(12):1256-1269.
49. Wise EA, Rosenberg PB, Lyketsos CG, Leoutsakos JM. Time course of neuropsychiatric symptoms and cognitive diagnosis in national Alzheimer's coordinating centers volunteers. *Alzheimers Dement*. 2019;11:333-339.
50. Cummings JL. The neuropsychiatric inventory: assessing psychopathology in dementia patients. *Neurology*. 1997;48:S10-S16.

51. Kaufer DI, Cummings JL, Ketchel P, et al. Validation of the NPI-Q, a brief clinical form of the neuropsychiatric inventory. *J Neuropsychiatry Clin Neurosci*. 2000;12:233-239.
52. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The neuropsychiatric inventory: comprehensive assessment of psychopathology in dementia. *Neurology*. 1994;44:2308-2314.
53. Reisberg B, Auer SR, Monteiro IM. Behavioral pathology in Alzheimer's disease (BEHAVE-AD) rating scale. *Int Psychogeriatr*. 1996;8:301-308.
54. Reisberg B, Monteiro I, Torossian C, et al. The BEHAVE-AD assessment system: a perspective, a commentary on new findings, and a historical review. *Dement Geriatr Cogn Disord*. 2014;38:89-146.
55. Sheikh JI, Yesavage JA. *Geriatric Depression Scale (GDS): Recent Evidence and Development of a Shorter Version*. The Haworth Press; 1986:165-173.
56. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16:606-613.
57. Hopko DR, Stanley MA, Reas DL, et al. Assessing worry in older adults: confirmatory factor analysis of the Penn state worry questionnaire and psychometric properties of an abbreviated model. *Psychol Assess*. 2003;15:173-183.
58. Bradford A, Brenes GA, Robinson RA, et al. Concordance of self- and proxy-rated worry and anxiety symptoms in older adults with dementia. *J Anxiety Disord*. 2013;27:125-130.
59. Pachana NA, Byrne GJ, Siddle H, Koloski N, Harley E, Arnold E. Development and validation of the geriatric anxiety inventory. *Int Psychogeriatr*. 2007;19:103-114.
60. Yesavage JA, Rose TL, Lapp D. *Validity of the Geriatric Depression Scale in Subjects with Senile Dementia*. Veterans Administration Medical Clinic; 1981
61. Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Use of the Cornell scale in nondemented patients. *J Am Geriatr Soc*. 1988;36:230-236.
62. Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell scale for depression in dementia. *Biol Psychiatry*. 1988;23:271-284.
63. Cornelis E, Gorus E, Van Schelvergem N, De Vriendt P. The relationship between basic, instrumental, and advanced activities of daily living and executive functioning in geriatric patients with neurocognitive disorders. *Int J Geriatr Psychiatry*. 2019;34:889-899.
64. De Vriendt P, Gorus E, Cornelis E, Bautmans I, Petrovic M, Mets T. The advanced activities of daily living: a tool allowing the evaluation of subtle functional decline in mild cognitive impairment. *J Nutr Health Aging*. 2013;17:64-71.
65. Reuben DB, Laliberte L, Hiris J, Mor V. A hierarchical exercise scale to measure function at the advanced activities of daily living (AADL) level. *J Am Geriatr Soc*. 1990;38:855-861.
66. Brown PJ, Devanand DP, Liu X, Caccappolo E. Functional impairment in elderly patients with mild cognitive impairment and mild Alzheimer disease. *Arch Gen Psychiatry*. 2011;68:617-626.
67. Cruz-Orduna I, Bellon JM, Torrero P, et al. Detecting MCI and dementia in primary care: effectiveness of the MMS, the FAQ and the IQCODE. *Fam Pract*. 2012;29:401-406.
68. Juva K, Makela M, Erkinjuntti T, et al. Functional assessment scales in detecting dementia. *Age Ageing*. 1997;26:393-400.
69. Cromwell DA, Eagar K, Poulos RG. The performance of instrumental activities of daily living scale in screening for cognitive impairment in elderly community residents. *J Clin Epidemiol*. 2003;56:131-137.
70. Li M, Ng TP, Kua EH, Ko SM. Brief informant screening test for mild cognitive impairment and early Alzheimer's disease. *Dement Geriatr Cogn Disord*. 2006;21:392-402.
71. Pfeffer RI, Kurosaki TT, Harrah CH Jr, Chance JM, Filos S. Measurement of functional activities in older adults in the community. *J Gerontol*. 1982;37:323-329.
72. Sikkes SA, de Lange-de Klerk ES, Pijnenburg YA, et al. A new informant-based questionnaire for instrumental activities of daily living in dementia. *Alzheimers Dement*. 2012;8:536-543.
73. Sikkes SA, Knol DL, Pijnenburg YA, de Lange-de Klerk ES, Uitdehaag BM, Scheltens P. Validation of the Amsterdam IADL questionnaire(c), a new tool to measure instrumental activities of daily living in dementia. *Neuroepidemiology*. 2013;41:35-41.
74. Sikkes SA, Pijnenburg YA, Knol DL, de Lange-de Klerk ES, Scheltens P, Uitdehaag BM. Assessment of instrumental activities of daily living in dementia: diagnostic value of the Amsterdam instrumental activities of daily living questionnaire. *J Geriatr Psychiatry Neurol*. 2013;26:244-250.
75. Jutten RJ, Peeters CFW, Leijdesdorff SMJ, et al. Detecting functional decline from normal aging to dementia: development and validation of a short version of the Amsterdam IADL questionnaire. *Alzheimers Dement*. 2017;8:26-35.
76. Koster N, Knol DL, Uitdehaag BM, Scheltens P, Sikkes SA. The sensitivity to change over time of the Amsterdam IADL questionnaire. *Alzheimers Dement*. 2015;11:1231-1240.
77. Hughes CP, Berg L, Danziger WL, Coben LA, Martin RL. A new clinical scale for the staging of dementia. *Br J Psychiatry*. 1982;140:566-572.
78. Morris JC. The clinical dementia rating (CDR): current version and scoring rules. *Neurology*. 1993;43:2412-2414.
79. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. *Int Psychogeriatr*. 1997;9(1):173-176.
80. Reisberg B. Functional assessment staging (FAST). *Psychopharmacol Bull*. 1988;24:653-659.
81. Sclan SG, Reisberg B. Functional assessment staging (FAST) in Alzheimer's disease: reliability, validity, and ordinality. *Int Psychogeriatr*. 1992;4(1):55-69.
82. Reisberg B, Ferris SH, Franssen E. An ordinal functional assessment tool for Alzheimer's-type dementia. *Hosp Community Psychiatry*. 1985;36:593-595.
83. Reisberg B, Ferris SH, de Leon MJ, Crook T. The global deterioration scale for assessment of primary degenerative dementia. *Am J Psychiatry*. 1982;139:1136-1139.
84. Bucks RS, Ashworth DL, Wilcock GK, Siegfried K. Assessment of activities of daily living in dementia: development of the Bristol activities of daily living scale. *Age Ageing*. 1996;25:113-120.
85. Gelinas I, Gauthier L, McIntyre M, Gauthier S. Development of a functional measure for persons with Alzheimer's disease: the disability assessment for dementia. *Am J Occup Ther*. 1999;53:471-481.
86. de Rotrou J, Wu YH, Hugonot-Diener L, et al. DAD-6: a 6-Item version of the disability assessment for dementia scale which may differentiate Alzheimer's disease and mild cognitive impairment from controls. *Dement Geriatr Cogn Disord*. 2012;33:210-218.
87. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9:179-186.
88. Cullen B, O'Neill B, Evans JJ, Coen RF, Lawlor BA. A review of screening tests for cognitive impairment. *J Neurol Neurosurg Psychiatry*. 2007;78:790-799.
89. Lin JS, O'Connor E, Rossom RC, Perdue LA, Eckstrom E. Screening for cognitive impairment in older adults: a systematic review for the U.S. preventive services task force. *Ann Intern Med*. 2013;159:601-612.
90. Tsoi KK, Chan JY, Hirai HW, Wong SY, Kwok TC. Cognitive tests to detect dementia: a systematic review and meta-analysis. *JAMA Intern Med*. 2015;175:1450-1458.
91. Berman SE, Koscik RL, Clark LR, et al. Use of the quick dementia rating system (QDRS) as an initial screening measure in a

longitudinal cohort at risk for Alzheimer's disease. *J Alzheimers Dis Rep*. 2017;1:9-13.
92. California Alzheimer's Disease Centers. Assessment of Cognitive Complaints Toolkit for Alzheimer's Disease. Self published, 2018
93. National Institute on Aging. Alzheimer's and Related Dementias Resources for Professionals. https://www.nia.nih.gov/health/health-care-professionals-information/alzheimers-and-related-dementias-resources
94. American Academy of Family Physicians. Cognitive Evaluation. https://www.aafp.org/family-physician/patient-care/care-resources/cognitive-care/cognitive-evaluation.html
95. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet commission. *Lancet*. 2020;396:413-446.
96. Agrawal Y, Platz EA, Niparko JK. Prevalence of hearing loss and differences by demographic characteristics among US adults: data from the national health and nutrition examination survey, 1999-2004. *Arch Intern Med*. 2008;168:1522-1530.
97. Chou R, Dana T, Bougatsos C, Grusing S, Blazina I. *Screening for Impaired Visual Acuity in Older Adults: A Systematic Review to Update the 2009 U.S.* Preventive Services Task Force Recommendation; 2016
98. Beauchet O, Annweiler C, Callisaya ML, et al. Poor gait performance and prediction of dementia: results from a meta-analysis. *J Am Med Dir Assoc*. 2016;17:482-490.
99. Montero-Odasso M, Speechley M. Falls in cognitively impaired older adults: implications for risk assessment and prevention. *J Am Geriatr Soc*. 2018;66:367-375.
100. Boeve BF, Molano JR, Ferman TJ, et al. Validation of the mayo sleep questionnaire to screen for REM sleep behavior disorder in an aging and dementia cohort. *Sleep Med*. 2011;12:445-453.
101. Marinus J, Visser M, van Hilten JJ, Lammers GJ, Stiggelbout AM. Assessment of sleep and sleepiness in Parkinson disease. *Sleep*. 2003;26:1049-1054.
102. Shprecher DR, Adler CH, Zhang N, et al. Predicting alpha-synuclein pathology by REM sleep behavior disorder diagnosis. *Parkinsonism Relat Disord*. 2018;55:92-96.
103. Boeve BF, Silber MH, Ferman TJ, et al. Clinicopathologic correlations in 172 cases of rapid eye movement sleep behavior disorder with or without a coexisting neurologic disorder. *Sleep Med*. 2013;14:754-762.
104. Boeve BF. Idiopathic REM sleep behaviour disorder in the development of Parkinson's disease. *Lancet Neurol*. 2013;12:469-482.
105. Winer JR, Mander BA, Kumar S, et al. Sleep disturbance forecasts β-amyloid accumulation across subsequent years. *Curr Biol*. 2020;30(21):4291-4298.e3.
106. Naismith SL, Mowszowski L. Sleep disturbance in mild cognitive impairment: a systematic review of recent findings. *Curr Opin Psychiatry*. 2018;31:153-159.
107. Davies CR, Harrington JJ. Impact of obstructive sleep apnea on neurocognitive function and impact of continuous positive air pressure. *Sleep Med Clin*. 2016;11:287-298.
108. Peterson K, Hahn H, Lee AJ, Madison CA, Atri A. In the information age, do dementia caregivers get the information they need? semi-structured interviews to determine informal caregivers' education needs, barriers, and preferences. *BMC Geriatr*. 2016;16(1):164
109. Folstein M, Folstein S, McHugh PR. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12:189-198.
110. Folstein MF, Robins LN, Helzer JE. The mini-mental state examination. *Arch Gen Psychiatry*. 1983;40:812
111. Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The mini-cog: a cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *Int J Geriatr Psychiatry*. 2000;15:1021-1027.
112. Brodaty H, Pond D, Kemp NM, et al. The GPCOG: a new screening test for dementia designed for general practice. *J Am Geriatr Soc*. 2002;50:530-534.
113. Tariq SH, Tumosa N, Chibnall JT, Perry MH 3rd, Morley JE. Comparison of the Saint Louis University mental status examination and the mini-mental state examination for detecting dementia and mild neurocognitive disorder–a pilot study. *Am J Geriatr Psychiatry*. 2006;14:900-910.
114. Hsieh S, McGrory S, Leslie F, et al. The mini-Addenbrooke's cognitive examination: a new assessment tool for dementia. *Dement Geriatr Cogn Disord*. 2015;39:1-11.
115. Katzman R, Brown T, Fuld P, Peck A, Schechter R, Schimmel H. Validation of a short orientation-memory-concentration test of cognitive impairment. *Am J Psychiatry*. 1983;140:734-739.
116. Buschke H, Kuslansky G, Katz M, et al. Screening for dementia with the memory impairment screen. *Neurology*. 1999;52:231-238.
117. Qureshi KN, Hodkinson HM. Evaluation of a ten-question mental test in the institutionalized elderly. *Age Ageing*. 1974;3:152-157.
118. Saliba D, Buchanan J, Edelen MO, et al. MDS 3.0: brief interview for mental status. *J Am Med Dir Assoc*. 2012;13:611-617.
119. Rouleau I, Salmon DP, Butters N, Kennedy C, McGuire K. Quantitative and qualitative analyses of clock drawings in Alzheimer's and Huntington's disease. *Brain Cogn*. 1992;18:70-87.
120. Froehlich TE, Robison JT, Inouye SK. Screening for dementia in the outpatient setting: the time and change test. *J Am Geriatr Soc*. 1998;46:1506-1511.
121. Solomon PR, Hirschoff A, Kelly B, et al. A 7 minute neurocognitive screening battery highly sensitive to Alzheimer's disease. *Arch Neurol*. 1998;55:349-355.
122. Tang-Wai DF, Knopman DS, Geda YE, et al. Comparison of the short test of mental status and the mini-mental state examination in mild cognitive impairment. *Arch Neurol*. 2003;60:1777-1781.
123. Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *Br J Psychiatry*. 1968;114:797-811.
124. Roth M, Tym E, Mountjoy CQ, et al. CAMDEX: a standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. *Br J Psychiatry*. 1986;149:698-709.
125. Hsieh S, Schubert S, Hoon C, Mioshi E, Hodges JR. Validation of the Addenbrooke's cognitive examination III in frontotemporal dementia and Alzheimer's disease. *Dement Geriatr Cogn Disord*. 2013;36:242-250.
126. Dubois B, Slachevsky A, Litvan I, Pillon B. The FAB: a frontal assessment battery at bedside. *Neurology*. 2000;55:1621-1626.
127. Blumenfeld H. *Neuroanatomy Through Clinical Cases*. Oxford University Press; 2021
128. Education JS. Physical Examinations III
129. Milligan TA. Diagnosis in neurologic disease. *Med Clin North Am*. 2019;103:173-190.
130. Creavin ST, Wisniewski S, Noel-Storr AH, et al. Mini-Mental state examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations. *The Cochrane Database of Sys Rev*. 2016;2016(1):Cd011145
131. Holsinger T, Deveau J, Boustani M. Does this patient have dementia?. *JAMA*. 2007;297:2391-2404.
132. Pinto TCC, Machado L, Bulgacov TM, et al. Is the Montreal cognitive assessment (MoCA) screening superior to the mini-mental state examination (MMSE) in the detection of mild cognitive impairment (MCI) and Alzheimer's disease (AD) in the elderly?. *Int Psychogeriatr*. 2019;31:491-504.
133. Julayanont P, Brousseau M, Chertkow H, Phillips N, Nasreddine ZS. Montreal cognitive assessment memory index score

(MoCA-MIS) as a predictor of conversion from mild cognitive impairment to Alzheimer's disease. *J Am Geriatr Soc*. 2014;62:679-684.
134. Kaur A, Edland SD, Peavy GM. The MoCA-memory index score: an efficient alternative to paragraph recall for the detection of amnestic mild cognitive impairment. *Alzheimer Dis Assoc Disord*. 2018;32:120-124.
135. Wood JL, Weintraub S, Coventry C, et al. Montreal cognitive assessment (MoCA) performance and domain-specific index scores in amnestic versus aphasic dementia. *J Int Neuropsychol Soc*. 2020;26:927-931.
136. Goldstein FC, Milloy A, Loring DW. Incremental validity of Montreal cognitive assessment index scores in mild cognitive impairment and Alzheimer disease. *Dement Geriatr Cogn Disord*. 2018;45:49-55.
137. Sheehan B. Assessment scales in dementia. *Ther Adv Neurol Disord*. 2012;5:349-358.
138. Shaughnessy L, Sheard S, Goldfarb D, Atri A. Cognitive assessment of Alzheimer's disease and dementias in clinical practice: pragmatics of brief instruments and neuropsychological evaluation. *J Clin Psychiatry*. 2019:80(4):MS18002BR2C
139. De Roeck EE, De Deyn PP, Dierckx E, Engelborghs S. Brief cognitive screening instruments for early detection of Alzheimer's disease: a systematic review. *Alzheimers Res. Ther*. 2019;11:21
140. Daffner KR, Gale SA, Barrett AM, et al. Improving clinical cognitive testing: report of the AAN behavioral neurology section workgroup. *Neurology*. 2015;85:910-918.
141. Tanev KS, Camprodon JA, Caplan DN, et al. Telemedicine-Based Cognitive Examinations During COVID-19 and Beyond: Perspective of the Massachusetts General Hospital Behavioral Neurology & Neuropsychiatry Group. *J Neuropsychiatry Clin Neurosci*. 2024;36:87-100.
142. Sano M, Zhu CW, Kaye J, et al. A randomized clinical trial to evaluate home-based assessment of people over 75 years old. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2019;15:615-624.
143. Brandt J, Spencer M, Folstein M. The Telephone Interview for Cognitive Status. *Neuropsychiatry Neuropsychol Behav Neurol*. 1988;1:111-117.
144. Brearly TW, Shura RD, Martindale SL, et al. Neuropsychological Test Administration by Videoconference: A Systematic Review and Meta-Analysis. *Neuropsychol Rev*. 2017;27:174-186.
145. Fong TG, Fearing MA, Jones RN, et al. Telephone interview for cognitive status: Creating a crosswalk with the Mini-Mental State Examination. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2009;5:492-497.
146. Wittich W, Phiillps N, Nasreddine Z, Chertikow H. Sensitivity and Specificity of the Montreal Cognitive Assessment Modified for Individuals Who Are Visually Impaired. *J Vis Impair Blin*. 2010:360-368.
147. DeYoung N, Shenal BV. The reliability of the Montreal Cognitive Assessment using telehealth in a rural setting with veterans. *J Telemed Telecare*. 2019;25:197-203.
148. Iiboshi K, Yoshida K, Yamaoka Y, et al. A Validation Study of the Remotely Administered Montreal Cognitive Assessment Tool in the Elderly Japanese Population. *Telemed J E Health*. 2020;26:920-928.
149. Roccaforte WH, Burke WJ, Bayer BL, Wengel SP. Validation of a telephone version of the mini-mental state examination. *J Am Geriatr Soc*. 1992;40:697-702.
150. Kennedy RE, Williams CP, Sawyer P, Allman RM, Crowe M. Comparison of in-person and telephone administration of the Mini-Mental State Examination in the University of Alabama at Birmingham Study of Aging. *J Am Geriatr Soc*. 2014;62:1928-1932.
151. Newkirk LA, Kim JM, Thompson JM, Tinklenberg JR, Yesavage JA, Taylor JL. Validation of a 26-point telephone version of the Mini-Mental State Examination. *J Geriatr Psychiatry Neurol*. 2004;17:81-87.
152. Cullum CM, Weiner MF, Gehrmann HR, Hynan LS. Feasibility of telecognitive assessment in dementia. *Assessment*. 2006;13:385-390.
153. Galusha-Glasscock JM, Horton DK, Weiner MF, Cullum CM. Video Teleconference Administration of the Repeatable Battery for the Assessment of Neuropsychological Status. *Arch Clin Neuropsychol*. 2016;31:8-11.
154. Wadsworth HE, Dhima K, Womack KB, Hart J, Jr., Weiner MF, Hynan LS, Cullum CM. Validity of Teleneuropsychological Assessment in Older Patients with Cognitive Disorders. *Arch Clin Neuropsychol*. 2018;33:1040-1045.
155. Harrell KM, Wilkins SS, Connor MK, Chodosh J. Telemedicine and the evaluation of cognitive impairment: the additive value of neuropsychological assessment. *J Am Med Dir Assoc*. 2014;15:600-606.
156. Dickerson BC, et al. The Alzheimer's association clinical practice guideline for the diagnostic evaluation, testing, counseling and disclosure of suspected Alzheimer's disease and related disorders (DETeCD-ADRD): Executive summary of recommendations for specialty care. *Alzheimer's Dement*. in press. doi:10.1002/alz.14337

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Atri A, Dickerson BC, Clevenger C, et al. The Alzheimer's Association clinical practice guideline for the diagnostic evaluation, testing, counseling, and disclosure of suspected Alzheimer's disease and related disorders (DETeCD-ADRD): Validated clinical assessment instruments. *Alzheimer's Dement*. 2024;1-20.
https://doi.org/10.1002/alz.14335