Alzheimer's & Dementia
Translational Research & Clinical Interventions

SPECIAL TOPIC SECTION

CCCDTD5 recommendations on early and timely assessment of neurocognitive disorders using cognitive, behavioral, and functional scales

David F. Tang-Wai[1] | **Eric E. Smith**[2] | **Marie-Andrée Bruneau**[3] | **Amer M. Burhan**[4] | **Atri Chatterjee**[5] | **Howard Chertkow**[6] | **Samira Choudhury**[7] | **Ehsan Dorri**[8] | **Simon Ducharme**[9] | **Corinne E. Fischer**[10] | **Sheena Ghodasara**[11] | **Nathan Herrmann**[12] | **Ging-Yuek Robin Hsiung**[5] | **Sanjeev Kumar**[13] | **Robert Laforce Jr**[14] | **Linda Lee**[15] | **Fadi Massoud**[16] | **Kenneth I. Shulman**[12] | **Michael Stiffel**[17] | **Serge Gauthier**[18] | **Zahinoor Ismail**[19]

[1] Department of Medicine, Divisions of Neurology and Geriatric Medicine, University of Toronto, University Health Network Memory Clinic, Krembil Brain Institute, Toronto, Ontario, Canada

[2] Department of Clinical Neurosciences and Hotchkiss Brain Institute, University of Calgary, Calgary, Alberta, Canada

[3] Department of Psychiatry and Addictology, University of Montreal, Geriatric Institute of Montreal Research Center, Montreal, Quebec, Canada

[4] Department of Psychiatry, Schulich School of Medicine and Dentistry, Western University; and Parkwood Institute-Mental Health, London, Ontario, Canada

[5] Division of Neurology, University of British Columbia, Vancouver, British Columbia, Canada

[6] Department of Medicine Neurology, Rotman Research Institute, University of Toronto, Toronto, Ontario, Canada

[7] Centre for Addiction and Mental Health, University of Toronto, Toronto, Ontario, Canada

[8] Department of Psychiatry, University of Alberta, Edmonton, Alberta, Canada

[9] Department of Psychiatry, Montreal QC, McConnell Brain Imaging, McGill University Health Centre, McGill University, Montreal Neurological Institute, Montreal, Quebec, Canada

[10] Keenan Research Centre for Biomedical Science, St. Michael's Hospital, Li Ka Shing Knowledge Institute, University of Toronto, Toronto, Ontario, Canada

[11] Department of Psychiatry, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada

[12] Sunnybrook Health Sciences Centre, Department of Psychiatry, University of Toronto, Toronto, Ontario, Canada

[13] Centre for Addiction and Mental Health, University of Toronto, Toronto, Ontario, Canada

[14] Clinique Interdisciplinaire de Mémoire, Département des Sciences Neurologiques, CHU de Québec, Université Laval, Quebec, Canada

[15] Department of Family Medicine, McMaster University, Hamilton, Ontario, Canada

[16] Centre Hospitalier Charles LeMoyne and Institut Universitaire de Gériatrie de Montréal, Department of Medicine, University of Sherbrooke and Department of Medicine, University of Montreal, Montreal, Quebec, Canada

[17] Université de Sherbrooke, Sherbrooke, Quebec, Canada

[18] McGill Center for Studies in Aging, Alzheimer Disease Research Unit, Montreal, Quebec, Canada

[19] Departments of Psychiatry, Clinical Neurosciences, Community Health Sciences, Hotchkiss Brain Institute and O'Brien Institute for Public Health, University of Calgary, Calgary, Alberta, Canada

Correspondence
Zahinoor Ismail, 3280 Hospital Dr. NW, TRW Building 1st Floor, Calgary, Alberta, Canada T2N 4Z6.
E-mail: ismailz@ucalgary.ca

Abstract

Introduction: Earlier diagnosis of neurocognitive disorders and neurodegenerative disease is needed to implement preventative interventions, minimize harm, and reduce risk of exploitation in the context of undetected disease. Along the spectrum from subjective cognitive decline (SCD) to dementia, evidence continues to emerge with respect to detection, staging, and monitoring. Updates to previous guidelines are required for clinical practice.

Methods: A subcommittee of the 5th Canadian Consensus Conference on Diagnosis and Treatment of Dementia (CCCDTD) reviewed emerging evidence to address the following: (1) Is there a role for screening at-risk patients without clinical concerns? In what context is assessment for dementia appropriate? (2) What tools can be used to evaluate patients in whom cognitive decline is suspected? (3) What important information can be gained from an informant, using which measures? (4) What instruments can be used to get more in-depth information to diagnose mild cognitive impairment (MCI) or dementia? (5) What is the approach to those with cognitive concerns but without objective changes (ie, SCD)? (6) How do we track response to treatment and change over time? The Grading of Recommendations Assessment, Development, and Evaluation system was used to rate quality of the evidence and strength of the recommendations.

Results: We recommend instruments to assess and monitor cognition, behavior, and function across the cognitive spectrum, including reports from patient and informant. We recommend against screening asymptomatic older adults but recommend investigation for self- or informant reports of changes in cognition, emergence of behavioral or psychiatric symptoms, or decline in function or self-care. Standardized assessments should be used for cognitive and behavioral change that have sufficient validity for use in clinical practice.

Discussion: The CCCDTD5 provides evidence-based recommendations for detection, assessment, and monitoring of neurocognitive disorders. Although these guidelines were developed for use in Canada, they may also be useful in other jurisdictions.

KEYWORDS

behavior, case finding, dementia, detection, function, guidelines, mild cognitive impairment, neuropsychiatric symptoms, SCD, screening

1 | INTRODUCTION

Detection of dementia remains an important goal in the care of older adults. However, the field has evolved over the past three decades with the identification of earlier stages of cognitive, behavioral, and functional changes in patients that occur years prior to an eventual dementia diagnosis. Consequently, the approaches to cognitive, behavioral, and functional assessments in both primary and specialty care settings have similarly evolved. Since 1989, five Canadian Consensus Conferences on the Diagnosis and Treatment of Dementia (CCCDTD)[1] have been conducted to reflect the ongoing advances with evidence-based recommendations.

The first CCCDTD, published in 1991,[2] recommended use of the Mini-Mental State Examination (MMSE)[3] as a suitable screening instrument to complement clinical history in the diagnosis and treatment of Alzheimer's disease (AD) and related dementias. CCCDTD2, published in 1999,[4] emphasized the importance of obtaining collateral information from a reliable informant and recommended the addition of the Functional Activities Questionnaire (FAQ)[5] to the MMSE. Serial assessments were recommended to confirm diagnosis and monitor response to treatment.[4] Screening was recommended for only older adults with clear symptoms of dementia and not those with cognitive impairment no dementia. CCCDTD3 was published in 2008 as a series of case-based papers.[6] The concept of mild cognitive

impairment (MCI) was introduced,[7] and a slate of brief and medium-length instruments, including the Montreal Cognitive Assessment (MoCA),[8] were recommended for use in the detection of MCI and dementia.[9] In this third iteration of CCCDTD, behavioral changes were discussed in the context of management of both (1) mild to moderate dementia[10] with recommendations to use the The Neuropsychiatric Inventory Questionnaire (NPI-Q)[11] for measurement, and (2) in severe dementia with a focus on behavioral and psychological symptoms of dementia.[12] CCCDTD4, published in 2012,[13] did not update the 2008 recommendations regarding screening, case finding, and dementia detection. This necessitated a comprehensive update for the current iteration and in 2019 to 2020 the fifth CCCDTD (CCCDTD5) was conducted to comprehensively review and update guidelines for cognitive disorders, the summary of which has been published.[1] This paper reviews the development and rationale for the recommendations related to early and timely diagnosis of cognitive and behavioral impairment using screening cognitive, behavioral, and functional scales.

2 | METHODS

A CCCDTD5 subcommittee was formed to create screening guidelines, including Canadian experts representing the disciplines of neurology, psychiatry, geriatric medicine, and family medicine. Prior CCCDTD guidelines were reviewed to identify areas that required revision. New areas for recommendations were identified by expert knowledge.

Subcommittee members then performed targeted systematic literature searches (available on request) using PubMed (Medline) to address the following clinical questions: (1) Is there a role for screening at-risk patients without clinical concerns? In what context is assessment for dementia appropriate? (2) What tools can be used to evaluate patients in whom cognitive decline is suspected? (3) What important information can be gained from an informant, using which measures? (4) What instruments can be used to get more in-depth information to diagnose MCI or dementia? (5) What is the approach to those with cognitive concerns but without objective changes (ie, recommendations for subjective cognitive decline [SCD])? (6) How do we track response to treatment and change over time?

Systematic reviews and important individual studies were included. Guidelines were drafted by committee members and the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was used to describe the strength of recommendation and quality of evidence (Table 1).[14] Recommendations were reviewed and revised until internal subcommittee consensus was obtained. All subcommittee recommendations were then voted on by all CCCDTD5 conference attendees, with a majority of 80% or higher required to pass. The final set of recommendations were presented at the CCCDTD5 steering committee meeting, in the presence of external observers and stakeholders, in Quebec City on October 3, 2019, for ratification and approval for publication.[1]

RESEARCH IN CONTEXT

1. **Systematic review**: Using expert knowledge and review of previous guidelines published in English and French, the committee identified six clinical questions for guideline development. A search strategy was created for each question and executed in August 2019 using PubMed (Medline) database.

2. **Interpretation**: We offer guidelines to the practicing clinician in the evaluation for diagnosis and follow-up of patients presenting with cognitive, functional, and behavioral symptoms. We provide an algorithmic approach to diagnostic assessment, including information from the patient and informant or care partner.

3. **Future directions**: Additional research is required on how these guidelines influence clinical practice and result in earlier or more accurate diagnosis of neurocognitive disorders. The supporting evidence is of variable quality, so future research may change these guidelines. In the future, technological and ecological assessments, including virtual assessments, may assist in dementia detection and monitoring.

HIGHLIGHTS

- We do not recommend cognitive screening in older adults unless there are cognitive symptoms or concerns.
- History from a reliable informant or care partner is a fundamental component in diagnostic assessment for cognitive concerns.
- We do recommend assessment and work-up in the case of change in cognition, emergence of behavioral or psychiatric symptoms, decline in function or self-care, victimization by financial scams, decline in driving abilities, new rambling or tangential history, difficulty following medical instructions or organizing medications, or missing appointments with increasing frequency.
- We provide recommendations for instruments administered to patient, and completed by informant/care partner, to assess cognition, behavior, and function across the spectrum from subjective cognitive decline to dementia.

3 | APPROACH

Clinicians see patients with a range of cognitive impairment (from none to frank impairment), mood and behavior symptoms (from none to severe dementia-related behaviors), and functional abilities (from independent to completely dependent). Attempts to make a satisfactory

TABLE 1 Evidence grading system

Strength of recommendation	1	Strong: benefits clearly outweigh undesirable effects
	2	Weak, or conditional: either lower quality evidence or desirable and undesirable effects are more closely balanced
Quality of evidence	A	High: "further research is unlikely to change confidence in the estimate of effect"
	B	Moderate: "further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate"
	C	Low: "further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate"

Note: Strength and quality levels are based on the GRADE system.[14]

diagnosis and plan may appear daunting as the number of the possible combinations from these changes appear infinite. These guidelines provide a practical approach to the evaluation by placing them into identifiable and manageable diagnostic groups by asking three simple questions: (1) Does the patient and/or informant complain of a behavior and/or cognitive change? (2) Are there objective changes in behavior and/or cognition? and (3) Is additional detailed cognitive testing required? For each question, the answer is either "yes" or a "no." Depending on the yes/no answer, a specific recommendation is then applied. Each recommendation, with supportive evidence, is framed around common clinical questions seen in practice. Figure 1 provides the illustrative demonstration of the flow of the clinical decisions, when and which recommendation to use, and how to follow a patient. With

respect to terminology, mild neurocognitive disorder and MCI are used interchangeably, as are major neurocognitive disorder and dementia.

Caveat: Clinicians should determine what is feasible in their setting when it comes to choosing the scales as some instruments require potential fees and/or training requirements. If fees or training requirements preclude using an instrument, other validated instruments can be chosen. The most important principle is *measurement-based care*, using all potential sources of information, which necessitates the use of a validated instrument, even if it is not one listed here.

4 | CCCDTD5 TOPICS

4.1 | Is there a role for screening at-risk patients without clinical concerns? In what context is assessment for dementia appropriate?

Dementia is often not recognized by primary care providers. A systematic review of epidemiological surveys found that in North America 63.6% of dementia cases were undetected as evidenced by an absence of a dementia diagnosis in the medical record.[15] Earlier recognition of cognitive impairment has many potential benefits such as allowing access to resources allowing patients to function better in the community; facilitating advance care planning; allowing earlier prescription of cholinesterase inhibitors for eligible patients; and fostering early discussions around harm reduction, such as stopping unsafe driving. On the other hand, there are potential risks related to administering cognitive tests to *asymptomatic* persons for signs of unrecognized dementia (ie, screening). With a low prevalence (6.8% in persons >60 years[16]) and only moderately high specificity for cognitive screening tests (90% for MMSE[16] and 87% for the MoCA[8]), the number of false positive
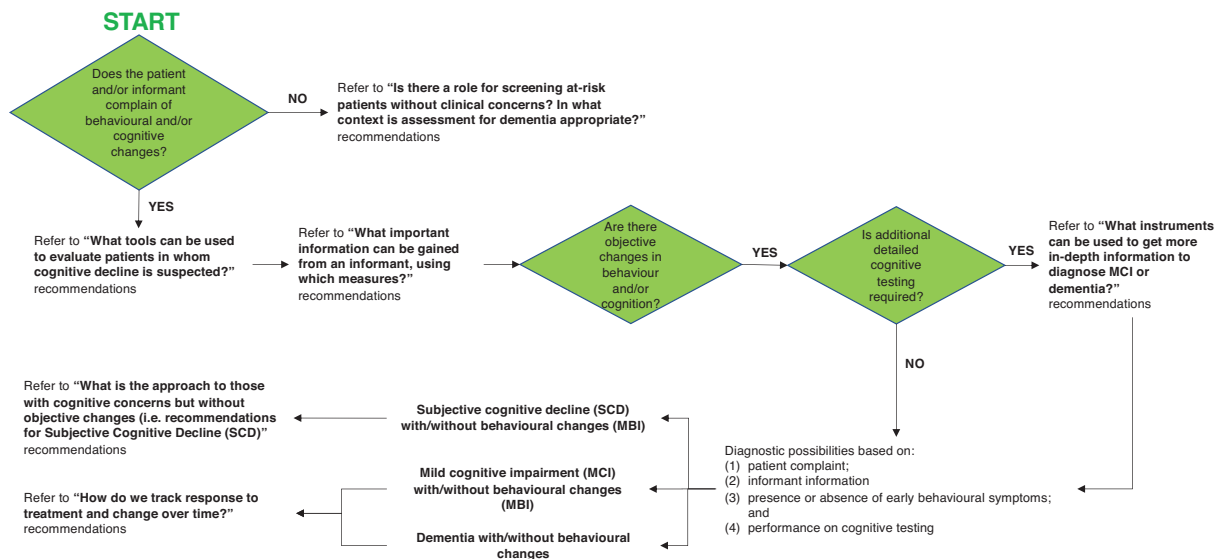

CCCDTD5 – Initial Assessment Flowchart

FIGURE 1 Flow of clinical decisions. MBI, mild behavioral impairment; BPSD, behavioral and psychological symptom of dementia

TABLE 2 Canadian Consensus Conference on Diagnosis and Treatment of Dementia 5 (CCCDTD5) recommendations for screening asymptomatic older adults, and in what context assessment for dementia is appropriate

Recommendation	Grade
1. Cognitive testing to screen asymptomatic adults for the presence of mild cognitive impairment or dementia, including asymptomatic persons with risk factors such as family history or vascular risk factors, is not recommended.	1C
2. Primary care health professionals should be vigilant for potential symptoms of cognitive disorders in older or at-risk individuals, including but not limited to: reported cognitive symptoms by the patient or an informant, otherwise unexplained decline in instrumental activities of living, missed appointments or difficulty remembering or following instructions or taking medications, decrease in self-care, victimized by financial scams, or new onset later-life behavioral changes including new depression or anxiety.	1C
If there is a clinical concern for a cognitive disorder (which may not always be shared by the patient due to anosognosia or denial) then validated assessments of cognition, activities of daily living, and neuropsychiatric symptoms are indicated (see subsequent sections for suggestions for valid tools).	1A
3. In persons at elevated risk for cognitive disorders (such as very advanced age, pre-existing brain diseases such as Parkinson's disease, a recent episode of delirium, or risk factors such as diabetes) it is reasonable to ask the patient (and an informant, if available) about concerns regarding memory.	2C
If clinically significant memory concerns are elicited then further evaluation using validated assessments of cognition, behavior, and function is appropriate (see subsequent sections for suggestions for valid tools).	1B

screens will exceed the number of true positives except in the highest risk patient populations, and will remain a problem even in very high risk patient populations. A systematic review found that the positive predictive value (that is, the percent of positive tests that are true positive and not false positives) would be as low as 20% in unselected persons age 65 to 74 and would only exceed 50% in persons 85 and older.[15] Millions of Canadians would need to be screened, cumulatively requiring a large amount of resources even for a brief 5- to 15-minute screening battery. The attitudes of patients to widespread screening is uncertain, and screening has risks for individuals. False positive screens could lead to psychological harm, anxiety, unnecessary and potentially invasive testing (eg, blood work and exposure to ionizing radiation for computed tomography), and stigmatization as a low cognitive performer. Screening has the potential to lead to loss of autonomy including loss of employment, revocation of driver's license, or potential loss of control over financial and other affairs, such that some patients may refuse consent to be screened or be disappointed or angry with the results.

Only one randomized controlled trial, the Indiana University Comparative Effectiveness of Dementia Screening (IU-CHOICE) trial, has evaluated the effects of cognitive screening in asymptomatic older adults.[17] In this trial, 4005 persons ≥65 years were randomized to either screening with the memory impairment screen and Mini-Cog or no screening. The authors reported no differences in anxiety or depression at 1 month, and no differences in health-related quality of life scores, health-care use, advance care planning, or AD diagnosis by physicians at 12 months after screening. Of those who screened positive, 62% declined follow-up by a specialty clinic for diagnostic assessment and preventive care.[17]

The role of cognitive screening in older adults has been examined by the United States Preventive Services Task Force[18] (USPSTF; revised in 2019 and recently published[19]) and the Canadian Task Force on Preventive Health Care in 2018.[20] They both concluded that there was insufficient evidence to recommend cognitive screening for asymptomatic older adults.

With the undefined benefits of screening, the certainty that screening would require significant resources and result in many false positive diagnoses, and the lack of endorsement by other guideline organizations, screening cannot be recommended based on current evidence (Table 2, Recommendation 1). This recommendation could be re-evaluated in the future if prospective good quality studies show that screening improves outcomes that are meaningful to patients and health systems (including improving a measure of quality of life or function at an acceptable cost).

However, to address the known under-recognition of dementia in the community, clinicians should be cognizant of the signs and symptoms of cognitive decline. Because of anosognosia, cultural expectations around memory and aging, or denial of symptoms, individuals and sometimes even their informants may not report symptoms of cognitive decline even when dementia is present. Certainly, attention should also be paid to the reports of the informant if s/he does observe cognitive, functional, or behavioral changes. In contrast to asymptomatic screening, clinicians should consider evaluating for dementia when other potential warning signs are present (Table 2, Recommendations 2 and 3), such as otherwise unexplained loss of function, decrease in self-care, new rambling or tangential history, or difficulty following medical instructions or organizing medications. Cognitive decline may be accompanied or preceded by new onset later-life psychiatric or behavioral disorders. In patients that have risk factors for dementia (included but not limited to very advanced age, hearing loss, vascular risk factors, low early life education, and family history) it may be reasonable to ask (patient and informant) about concerns over memory loss, and then apply the recommendations as appropriate.

4.2 | What tools can be used to evaluate patients in whom cognitive decline is suspected?

Cognitive impairment is highly prevalent in the aging population as age is a major risk factor. Additionally, cognitive impairment may

be either the sequelae of medical conditions or an early harbinger of subsequent dementia. Although effective disease-modifying treatments for dementia do not yet exist, identifying cognitive impairment and/or dementia at the earliest possible phase may be beneficial to address potentially modifiable causes and to consider symptomatic treatments which do have modest efficacy in the early stages.[21]

Given the absence of reliable and/or easily available biomarkers for diagnosis, early detection often relies on *clinical* markers. Patients and/or family members can become aware of a change in the patient's cognition, behavior, or function, prompting a visit to the doctor who may administer cognitive testing and/or refer to a specialist for such an assessment. As access to specialty clinics may prove challenging due to the need to travel to major centers and/or prolonged wait times, the emphasis should be on administering brief cognitive tests.

As described in Recommendation 1 in Table 2, there are no data to support asymptomatic screening.[20] Nonetheless, primary care health professionals should stay vigilant for potential early symptoms of cognitive disorders in older individuals who may be less likely to report due to their lack of insight, social isolation, or sociocultural beliefs. Clinicians should also remain vigilant for changes in cognitive status in patients who are at risk for cognitive decline (Recommendations 2 and 3 in Table 2), including patients that are older. Conditions associated with elevated risk for cognitive disorders are: history of stroke or transient ischemic attack (TIA); late-onset depressive disorder or lifetime history of major depressive disorder; untreated sleep apnea; metabolic or cardiovascular morbidity; recent episode of delirium; first major psychiatric episode at an advanced age (psychosis, anxiety, mania); recent head injury; Parkinson's disease.[22] If there are early warning signs or clinical concerns for a cognitive disorder (Table 2—which may only be reported by a family member or loved one) then the complaint should be examined with a family member, and validated assessments of cognition, activities of daily living, and neuropsychiatric symptoms (NPS) are indicated.

The past few years have seen an exponential rise in the availability and widespread use of screening instruments; however, their ability to discriminate early cognitive changes is unclear.[23] Moreover, the value of combining instruments that gauge cognition, behavior, function, and subjective complaints that improves the clinician's ability to make an early diagnosis is not yet obvious from the literature. What is evident is that the instruments when used in isolation may not be very helpful to determine a diagnosis in the absence of adequate collateral history from a patient and an informant and appropriate investigations.[24] It is necessary to examine memory complaints with corroboration from an informant, conduct a focused clinical/neurological examination of the patient (including objective assessment of the patient's cognitive function, functional status and NPS using effective screening tools), and complement with laboratory tests.

Short assessment tools that screen patients for cognitive impairment are often desired over long test batteries for various reasons. First, they are less burdensome on patients, caregivers, and healthcare providers. Second, they provide crucial information about who may be at risk for cognitive decline or warrant further testing. Third, they may be more suitable if patients are not able to be tested in their primary language. Fourth, they can be easily administered in a family doctor's office and do not require engagement of tertiary clinics or referral to a specialist. These short tools include the Mini-Cog,[25] four-item version of MoCA[8] (Clock-drawing, Tap-at-letter-A, Orientation, and Delayed-recall), the Memory Impairment Screen (MIS),[26] the Clock Drawing Test (CDT),[27] and the General Practitioner Assessment of Cognition (GPCOG[28]). The Mini-Cog combines CDT plus 3-word-recall. It has shown comparable psychometric properties to the MMSE, but is less confounded by language and education, with a sensitivity of 39% to 84%[22] for detecting either MCI or dementia.[29] The MIS measures delayed free recall and cued memory using four items and is recommended for rapid screening of memory disorder. Its sensitivity is 43% to 86% and specificity from 93 to 97%.[30] The CDT is extremely simple to administer and extensively studied with a sensitivity of 67% to 98% and specificity of 69 to 94[30] for dementia screening but of around 60% sensitivity and specificity for MCI detection.[30]

Where time permits, slightly more detailed testing using such instruments as the Modified MMSE (3MS)[31] examination, MMSE, or Rowland Universal Dementia Assessment (RUDAS)[32] are preferred as they are more capable of detecting milder stages of cognitive impairment. The MMSE is widely used in many countries with excellent sensitivity and specificity and is useful in separating moderate dementia from normal cognition. However, it lacks sensitivity for the diagnosis of mild dementia or MCI. The MoCA is more sensitive (sensitivity for MCI: 80% to 100% and for dementia: 100%)[22] at discriminating early stage cognitive decline relative to the MMSE (sensitivity for MCI: 20% to 93% and for dementia: 81% to 93%).[22] The RUDAS is preferred in patients with limited English or limited education (Recommendation 6). The 3MS allows a more detailed cognitive evaluation than the MMSE with a sensitivity of about 86% and specificity of 79% for dementia.[33] The accuracy of screening tests may be optimized by conducting longitudinal assessments, like the QuoCo curves (www.quoco.org) which are similar to the concept of pediatric growth curves and are designed to optimize accuracy for distinguishing persons with dementia from healthy controls.[34]

Informant-rated tools focusing on cognitive and functional impairment may assist in the identification of dementia, particularly when time is limited or the patient is uncooperative, including questionnaires such as the Eight-Item Informant Interview to Differentiate Aging and Dementia (AD8;[35] sensitivity: 77% to 91%; specificity: 78% to 92%) or the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE;[36] sensitivity—MCI: 75% dementia: 75% to 81%; specificity—MCI: 69% dementia: 68% to 80%).[22] Moreover, improved rates of case finding can be achieved by combining cognitive screens with functional screens (such as the FAQ or the Disability Assessment for Dementia [DAD][37]) and informant-based measures. The FAQ is well-adapted for use in a primary care setting. It has been administered yearly to thousands of patients in Alzheimer's research centers in the United States.

Finally, there are emerging data suggesting that NPS are an early harbinger of dementia. Tools evaluating behavior, such as the NPI-Q[11], Mild Behavioral Impairment Checklist (MBI-C),[38] or Patient Health Questionnaire-9 (PHQ-9)[39] may be helpful. The NPI-Q assesses 12 dementia-related behavioral symptoms and has been validated in many

countries, shows high content validity for many specific symptoms, and inter-rater reliability (94% to 100%). The NPI-Q documents if each of the 12 subdomains is either present or absent and rates the presence or absence, and the severity of the symptoms on a 3-point scale, along caregiver distress on a 5-point scale. The PHQ-9 is part of a more global health assessment (PHQ) used for screening in primary care for the presence and severity of depressive symptoms. The MBI-C is a novel instrument developed by the NPS Professional Interest Area of the Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART-AA) as the case ascertainment instrument to measure mild behavioral impairment (MBI) in accordance with the ISTAART-AA MBI criteria.[38] MBI is characterized by later life onset of persistent NPS, as potential non-cognitive markers of cognitive decline and dementia. The five MBI domains[40] are: (1) decreased drive and motivation (apathy); (2) emotional dysregulation (mood and anxiety symptoms); (3) impulse dyscontrol (agitation, aggression, impulsivity, abnormal reward salience); (4) social inappropriateness (impaired social cognition); and (5) abnormal perception or thought content (psychotic symptoms), all of which are assessed with the MBI-C using the same 3-point measurement scale as the NPI-Q.[38] The recommendations are shown in Table 3.

4.3 | What important information can be gained from an informant, using which measures?

There are several barriers for the early and accurate diagnosis of neurocognitive disorders including limited patient insight.[41] Patients may deny their symptoms due to lack of insight[42] and may not be able to provide valid self-report about their illness. Further, the degree of impairment can impact insight and the reliability of the self-information.[43,44] Studies have found that collateral sources are likely to report more symptoms accurately than the patient themselves[45] and even though many guidelines highlight the importance of collateral information (since CCCDTD2 in 1999), implementation can be challenging and collection of collateral information remains relatively neglected in routine clinical practice.[46] This subcommittee identified several informant-based tools regarding the use of collateral information and studied their validity, reliability, and acceptability to clinicians and researchers. The strengths and weaknesses of individual tools are briefly discussed.

Several tools assessing both cognition and function through an informant report exist. The AD8 (described in Section 4.2) is a very useful instrument for differentiating dementia from normal aging. The Alzheimer's Questionnaire (AQ) is a 21-item tool and has shown sensitivity of 86% to 98% and a specificity of 94% to 96% for detection of MCI and AD.[47] The IQCODE has a short version and a long version that take 10 to 20 minutes to complete with sensitivity and specificity ranging from 75% to 100% depending on the cut-off used.[48] The Everyday Cognition (ECog)[49] is a tool used widely in research to obtain informant report about cognition. It also has short and long versions with administration times of 5 to 15 minutes and has up to 93% sensitivity and 80% specificity in detecting dementia. Other tools such as the Lawton,[50] the

Amsterdam Instrumental Activities of Daily Living Questionnaire (A-IADL-Q),[51] and the FAQ assess only function through informant report. Some tools such as Dementia Severity Rating Scale (DSRS)[52] and Quick Dementia Rating System (QDRS)[53] can be used to rate the stage of dementia based on informant report.

Some tools provide a measure of behavior based on informant report. The NPI[54] is the most widely used tool in research for comprehensive assessment of behavioral changes in neurocognitive disorders. It covers 12 domains and has 84 items, taking 30 to 45 minutes to complete, and the rating is based on informant report as well as direct observation of the patient. The NPI-Q is an informant rated version of the NPI (details described in the preceding section) that has shown excellent correlation with the full NPI and a high-test retest reliability. The MBI-C is a recently developed tool intended to assess emergent NPS in older adults with normal cognition,[40,55] SCD,[56] or MCI.[57] The MBI-C assesses five neuropsychiatric domains relevant to dementia care but is not yet well known to clinicians. The recommendations for informant-rated instruments are shown in Table 4.

4.4 | CCCDTD5 recommendations for what instruments can be used to get more in-depth information to diagnose MCI or dementia?

Clinical evaluation of cognitive complaints to make a diagnosis of either MCI or dementia requires the use of multiple modalities including a corroborative story from informants (care partners or family members), neurocognitive examination, basic biological tests, and brain imaging.[59-61] Multiple screening instruments exist for the evaluation of cognitive complaints in the context of MCI or dementia. In addition to instruments covered in Section 4.2, commonly known instruments include the Addenbrooke's Cognitive Examination (ACE),[62] Clinical Dementia Rating (CDR),[63] the Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog),[64] the Cambridge Cognition Examination (CAMCOG),[65] DemTect,[66] and Community Screening Instrument for Dementia.[67] All show very high diagnostic accuracy for dementia, with variable preferences and outcomes depending on the studies.[68] In differentiating MCI from dementia, the MoCA and Quick Mild Cognitive Impairment screen (QMCI)[69] are both accurate tools with one study favoring QMCI because of time and better accuracy for differentiating normal cognition from MCI.[70] However, many screening tools focus on deficits in anterograde memory for diagnosis—thus focusing mainly on either amnestic MCI or typical AD dementia—and do not adequately assess other cognitive domains that may also be affected. Additional in-depth cognitive instruments are required to determine other areas of impairment and/or determination of non-typical AD causes before a referral to memory clinic specialists can be planned. As described in Table 4, informant-rated questionnaires can complement scales administered to the patient or identify those warranting further investigation or evaluation.

Detailed neuropsychological testing can be obtained for additional information; however, this can be time consuming, not available to many physicians, and expensive if not covered. Several recent

TABLE 3 Canadian Consensus Conference on Diagnosis and Treatment of Dementia 5 (CCCDTD5) recommendations for what tools can be used to evaluate patients in whom cognitive decline is suspected

Recommendation	Grade
1. Routine screening of asymptomatic individuals has no evidence at this point. Cognitive testing to screen asymptomatic adults for the presence of mild cognitive impairment or dementia is not recommended.	1C
2. Primary care health professionals should stay vigilant for potential early symptoms of cognitive disorders in older individuals who may be less likely to report due their lack of insight, social isolation, or sociocultural beliefs, and in older individuals with warning signs, including but not limited to: reported cognitive symptoms by the patient or an informant, otherwise unexplained decline in instrumental activities of living, missed appointments, showing up to appointments at the incorrect time or day, difficulty remembering or following instructions or taking medications, decrease in self-care, or new onset of later-life behavioral changes including new depression or anxiety.	1C
If there is a clinical concern for a cognitive disorder (which may not always be shared by the patient due to their lack of insight) then validated assessments of cognition, activities of daily living, and neuropsychiatric symptoms are indicated (see subsequent sections for suggestions for valid tools).	1A
3. In persons with elevated risk for cognitive disorders or with medical conditions associated with cognitive disorders such as: (a) a history of stroke or transient ischemic attack (TIA); (b) late-onset depressive disorder or a lifetime history of major depressive disorder; (c) untreated sleep apnea; (d) unstable metabolic or cardiovascular morbidity; (e) a recent episode of delirium; (f) first major psychiatric episode at an advanced age (psychosis, anxiety, depression, mania); (g) recent head injury; (h) Parkinson's disease, it is reasonable to ask the patient and an informant about concerns regarding cognition and behavior.[22]	2C
If clinically significant cognitive concerns are elicited, then further evaluation using validated assessments of cognition, behavior, and function is appropriate (see subsequent sections for suggestions for valid tools).	1B
4. It is important to differentiate MCI from dementia and currently this distinction is made clinically on the basis of assessment of cognition and function. For screening purposes, examining the complaint with the patient and a family member and proceeding with an objective assessment of cognition and functional impairment should be done.	1A
5. An objective assessment of the patient's cognitive function could be achieved by using rapid psychometric screening tools such as the MIS + CDT, the Mini-Cog, the AD8, the four-item version of the MoCA (Clock-drawing, Tap-at-letter-A, Orientation, and Delayed-recall), and the GPCOG.	2B
6. If more time is allowed, preference should be given to using a more comprehensive psychometric screening tool the 3MS, MMSE, or RUDAS. The MMSE is widely used in many countries with excellent sensitivity and specificity and is useful in separating moderate dementia from normal cognition. However, it lacks sensitivity for the diagnosis of mild dementia or MCI. The MoCA relative to the MMSE is more sensitive to MCI and its use is often recommended when there is clinical suspicion of mild cognitive impairment or in cases where there is concern about the patient's cognitive status, and the MMSE score is in the "normal" range (24+ out of 30).	1B
7. The use of longitudinal serial cognitive assessments like the QuoCo curves might help optimize accuracy for distinguishing participants with dementia from healthy controls.	1C
8. To obtain information in addition to that provided by the other psychometric screening tools, or if the patient is unable to answer the questions on the screening tools (lack of time or uncooperative), having the caregiver complete a questionnaire for identifying a cognitive and/or functional change, such as the AD8 or IQCODE is recommended.	1B
9. Combining cognitive tests with functional screens and informant reports may improve case-finding in people with cognitive difficulties.	1A
10. Rapid screening of functional autonomy should be completed by an objective assessment with the patient and a family member using the FAQ or DAD.	1C
11. If a personality, behavior ,or mood change has been observed, an objective assessment of the behavioral and psychological symptoms of dementia (BPSD) with the patient and a family member using the NPI-Q, MBI-C or if a mood change has been observed with the PHQ-9.	1A

Abbreviations: 3MS, Modified Mini-Mental State Examination; AD8, Eight-Item Informant Interview to Differentiate Aging and Dementia; BPSD, behavioral and psychological symptom of dementia; DAD, Disability Assessment for Dementia; FAQ, Functional Activities Questionnaire; GPCOG, General Practitioner Assessment of Cognition; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MBI-C, Mild Behavioral Impairment Checklist; MCI, mild cognitive impairment; MIS, Memory Impairment Screen; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NPI-Q, The Neuropsychiatric Inventory Questionnaire; PHQ-9, Patient Health Questionnaire-9; RUDAS, Rowland Universal Dementia Assessment.

measures that are intermediate between screening tests and full neuropsychological testing have been developed. The Toronto Cognitive Assessment (TorCA) showed strong sensitivity/specificity to detect amnestic MCI.[71] Other authors have generated cognitive charts (QuoCo www.quoco.org) for use in clinical practice to assess longitudinal age-associated decline and have a sensitivity of 80% and a specificity of 89% for distinguishing healthy controls from participants with dementia.[34] Finally, a wide variety of other questionnaires exist for the detection of MCI but they have variable degrees of sensitivity/specificity depending on the differential diagnosis and cognitive domains explored.[72]

A recent trend in the field has been to develop cognitive screening tools for early recognition of atypical dementia syndromes. The Dépistage Cognitif de Québec (DCQ)[73] was developed based on updated criteria for AD and variants, primary progressive aphasia and behavioral variant frontotemporal dementia. This new tool showed excellent psychometric properties and was superior to the MoCA in a comparative study with a predictive power of 79% for

TABLE 4 Canadian Consensus Conference on Diagnosis and Treatment of Dementia 5 (CCCDTD5) recommendations for informant-rated instruments on cognition, function, and behavior

Recommendation	Grade
1. Due to variability in insight into cognitive, functional and behavioral changes, report from a reliable informant is an essential component for the assessment of patients with suspected neurocognitive disorders at all settings.	1C
2. The use of standardized tools to obtain informant report on changes in cognition, function, and behavior increases the diagnostic accuracy when combined with patient-related measures and therefore is recommended.	1C
3. We recommend using one or more informant-based tools that cover cognitive, functional, and behavioral aspects. Specific tools can be selected based on the need for comprehensive assessment versus efficiency depending upon the setting.	1C
4. There is ongoing development of informant-based tools, and based on the current evidence we recommend tools that: measure informant's report of cognitive changes (eg, ECog); measure informant's report on cognitive and functional changes (eg, AD8, IQCODE, QDRS); measure informant's report on functional changes combined with cognitive assessment as an alternative (eg, FAQ, 4-IADL,[58] A-IADL-Q); measure informant's report on behavioral changes (eg, NPI-Q, MBI-C).	1B

Abbreviations: AD8, Eight-Item Informant Interview to Differentiate Aging and Dementia; A-IADL-Q, Amsterdam Instrumental Activities of Daily Living Questionnaire; ECog, Everyday Cognition; FAQ, Functional Activities Questionnaire; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MBI-C, Mild Behavioral Impairment Checklist; NPI-Q, The Neuropsychiatric Inventory Questionnaire; QDRS, Quick Dementia Rating System.

TABLE 5 Canadian Consensus Conference on Diagnosis and Treatment of Dementia 5 (CCCDTD5) recommendations for more in-depth instruments to diagnose MCI or dementia

Recommendation	Grade
1. A number of well-validated instruments exist to help in the process of MCI or dementia diagnosis. However, diagnosis of MCI or dementia should not be solely based on an impaired result on cognitive screening tests.	1B
2. Cognitive screening tools exists specifically for the early identification of MCI (MoCA, TorCA). Among them, the MoCA offers strong normative data[78] (1C) while the TorCA has just been recently published.	1C 2B
3. Consider the DCQ, a new cognitive screening tool developed based on updated criteria for atypical syndromes (behavioral variant frontotemporal dementia, primary progressive aphasia, and Alzheimer's disease variants). It has been well validated in French and English and offers an option to commonly used screening tests (eg, MMSE, MoCA) which were not designed for screening atypical syndromes and are often not sufficient to capture subtle cognitive and social cognition changes associated with atypical dementia.	2B
4. Innovative new tools exist, similar to growth curves used in pediatrics, to allow longitudinal cognitive evaluation based on serial cognitive assessments.	1C

Abbreviations: DCQ, Dépistage Cognitif de Québec; MCI, mild cognitive impairment; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; TorCa, Toronto Cognitive Assessment.

the differentiation of atypical and typical dementias.[74] Other tests including computer-based models such as Helping Hand Technology assessment[75] have demonstrated promising results compared to current tools but require further evaluation in a clinical setting to determine their potential roles in the evaluation of cognitive disorders.[76,77]

In addition to neuropsychological testing (if available), recommendations are made with regard to the instruments available for more in-depth cognitive evaluation of MCI and dementia (see Table 5).

4.5 | What is the approach to SCD?

SCD, simply defined, is a condition in which a patient complains about their cognition but both their function and performance on objective cognitive testing are normal. While MCI has been well established as a transitional stage between normal cognition and dementia, and often reflects prodromal dementia, SCD has emerged as a potentially earlier manifestation of MCI and dementia, reflecting preclinical disease *in some*. Thus, from normal to dementia occurs on a cognitive continuum and there ought to be a "logical" progression of symptoms

starting from: (1) cognitive complaints, normal testing, normal function (SCD); then (2) cognitive complaints, "abnormal" testing, and relatively normal function (MCI); and (3) cognitive complaints, abnormal testing, and "abnormal" function (dementia). In light of this continuum, SCD is defined as a self-perceived decline in cognitive ability, associated with concerns, in the absence of objective findings.[79] In a study of older adults with SCD, 26% were determined to be amyloid beta (Aβ) positive.[80] A meta-analysis of studies following persons with SCD over time demonstrated progression to MCI in 27% of participants, and progression to dementia in 15%, over a mean of 4.8 years, with a risk of conversion to dementia about twice that of those without SCD.[81] Much of the SCD literature proposes SCD specifically as a pre-AD syndrome, similar to MCI in early iterations. It is possible, however, that SCD could be a precursor to other dementias as well. SCD is etiologically heterogeneous—in an SCD validation study, 25% had preclinical AD, 38% "subthreshold psychiatric issues," and 43% neither.[82] Thus, patients and families can be assured that SCD status alone does not automatically translate to a high risk of dementia.[83,84]

Psychiatric symptomatology, especially anxiety, depression, and personality features, can contribute to subjective cognitive changes,

TABLE 6 Canadian Consensus Conference on Diagnosis and Treatment of Dementia 5 (CCCDTD5) recommendations for the approach to subjective cognitive decline?

Recommendation	Grade
1. Patients presenting with consistent subjective cognitive complaints, with normal cognitive testing, in the absence of any obvious impairment in Instrumental Activities of Daily Living should undergo an appropriate diagnostic workup (ie, standard dementia medical workup to identify reversible causes, and psychiatric symptom assessment—with a special emphasis on depressive and anxious symptoms).	1B
2. Obtaining corroborative history is essential and has prognostic significance. Reliable informant information should be obtained for changes in cognition, function, and behavior/neuropsychiatric symptoms (ie, new onset symptoms vs chronic or longstanding symptoms).	1B
3. Use of structured scales for: objective cognition (eg, MoCA, CDT); subjective cognition (eg, SCD-Q part 1 (MyCog)[103]); informant reported cognition/function (eg, ECog, IQCODE, Lawton, PDQ,[104] SCD-Q part 2 [TheirCog][103]); and behavior (eg, informant report [MBI-C, NPI-Q] and self [GDS,[101] PHQ-9, GAD-7[102]]) is recommended.	1B
4. For patients with a negative corroborative history, reassurance should be provided, and follow-up offered if the patient or informant sources note deterioration in the future in any of the domains of cognition, function, or behavior.	2C
5. For patients with a positive corroborative history, annual follow-ups are recommended.	1B
6. For patients with a positive corroborative history, referral to a primary or specialty care memory clinic, and further investigation with laboratory testing, neuroimaging, detailed neuropsychiatric testing might be considered.	2C
7. Patients with SCD and significant psychiatric symptoms could be referred for psychiatric assessment and/or treatment, depending on the clinician's expertise.	1B
8. All patients presenting with SCD should be provided with information on the WHO recommendations for the prevention of dementia[105]	1C

Abbreviations: CDT, Clock Drawing Test; ECog, Everyday Cognition; GAD-7, Generalized Anxiety Disorder Screener; GDS, Geriatric Depression Scale; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MBI-C, Mild Behavioral Impairment Checklist; MoCA, Montreal Cognitive Assessment; NPI-Q, The Neuropsychiatric Inventory Questionnaire; PDQ, Personhood in Dementia Questionnaire; PHQ-9, Patient Health Questionnaire-9; SCD, subjective cognitive decline; SCD-Q, Subjective Cognitive Decline Questionnaire; WHO, World Health Organization.

and thus require assessment when evaluating SCD.[85-88] Important in this assessment is the distinction between chronic and recurrent psychiatric symptomatology, and new onset NPS in later life, the latter of which are more associated with incident cognitive decline and dementia.[55,89-98] New onset psychiatric and behavioral symptoms are reflected in the ISTAART-AA criteria for the MBI syndrome, in which later life onset of persistent NPS are a risk marker for dementia.[99] Recent evidence has demonstrated that in cognitively normal older adults, either SCD or MBI alone was associated with increased risk of incident MCI at 3 years, but the highest risk for progression was with the combination of SCD and MBI.[100] Thus, in addition to standard investigations (eg, blood work), assessing both neurobehavioral symptoms and subjective cognitive changes is essential to risk assessment and early detection. Assessments of behavior should include structured *informant-rated* scales such as the MBI-C or NPI-Q to systematically capture NPS. Self-reported or clinician-rated depression and anxiety scales may be administered to the patient—examples include the PHQ-9 mood scale, Geriatric Depression Scale (GDS),[101] and Generalized Anxiety Disorder Screener (GAD-7).[102] With that in mind, the recommendations for assessment of SCD in primary care and specialty care settings are listed in Table 6.

4.6 | How do we track response to treatment and change over time?

Monitoring change over time can be useful to evaluate the benefit of treatments including cholinesterase inhibitors (ChEI), anticipate care needs, and identify safety concerns. Various scales and tools to

TABLE 7 Optimal expectations with cognitive and mood/behavioral treatments at 6 to 12 months

Clinical domain	Expectation
Cognition	Stabilization or mild improvement (assess every 6 to 12 months)
Functional autonomy	Stabilization (assess every 6 to 12 months)
Behavior	Absence of new behavioral symptoms (assess every 3 to 6 months)
Global impression	Stabilization or mild improvement (assess every 6 to 12 months)

track cognitive, functional, behavioral, and global change over time and response to treatment have been used in clinical trials of ChEI (for mild to severe stages) and memantine (for moderate to severe stages). However, most of these tools are not familiar to the primary care physician and are not designed for use in clinical practice. It is therefore challenging to recommend objective measures to assess clinical response and progression of the disease.

Most, if not all, patients will experience clinical decline. However, it remains unclear how to appropriately make these assessments and determine what to expect once the patient starts declining clinically, given that assessing response to treatment is most often based on clinical judgment. The challenge is to determine the practical characterization of reasonable clinical outcomes and domains of measurement with symptomatic (ie, non disease-modifying) treatments in the face of a degenerative and progressive disease. Change over time should neither be assessed by a single tool nor in one clinical domain. Rather, it

TABLE 8 Recommended scales for assessment of clinical response to antidementia treatment

	Cognition	Functional autonomy	Behavior	Caregiver burden	Global impression
Research-based tools	ADAS-Cog	ADCS-ADL[107]	NPI	Zarit Burden Interview[110]	CIBIC-Plus
	SIB[106]	PDS[108]	BEHAVE-AD[109]		ADCS-CGIC[111]
					CDR
Practice-based tools	MMSE	DAD	NPI-Q	Zarit Burden Interview[110]	IQCODE
	sMMSE	FAST[112]	GDS		HABC-Monitor[116]
	3MS	FAQ	CSDD[115]		
	MoCA	OARS[113]	PHQ-9		
	RUDAS	Barthel[114]			
	CDT				

Abbreviations: 3MS, Modified Mini-Mental State Examination; ADAS-Cog, Alzheimer's Disease Assessment Scale-Cognitive; ADCS-ADL, Alzheimer's Disease Cooperative Study-Activities of Daily Living; ADAS-CGIC, Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change Scale; BEHAVE-AD, Behavioral Pathology in Alzheimer's Disease; CDR, Clinical Dementia Rating; CDT, Clock Drawing Test; CIBIC-Plus, Clinician's Interview-Based Impression of Change Plus Caregiver Input; CSDD, Cornell Scale for Depression in Dementia; DAD, Disability Assessment for Dementia; FAQ, Functional Activities Questionnaire; FAST, Functional Assessment Staging; GDS, Global Deterioration Scale; HABC-Monitor, Healthy Aging Brain Care Monitor; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NPI-Q, The Neuropsychiatric Inventory Questionnaire; PDS, Progressive Deterioration Scale; PHQ-9, Patient Health Questionnaire-9; OARS, Observved Affect Rating Scale; RUDAS, Rowland Universal Dementia Assessment; SIB, Severe Impairment Battery; sMMSE, Standardized Mini-Mental State Examination.

is recommended to proceed with a multi-dimensional approach with *major* emphasis on caregiver or reliable informant input (see Table 4). Experts usually agree that expectations are measurement at 6 to 12 months in the domains of cognition, function, behavior, and global impression[10] (Table 7).

Consistent with all CCCDTD5 recommendations, clinicians should determine what is feasible in their setting when it comes to choosing the instruments. The most important principle is measurement-based care, using all potential sources of information, which necessitates the use of a validated instrument, even if it is not one listed here. With these principles in mind, a summary of instruments is found in Table 8, and recommendations for tracking treatment response and change are found in Table 9.

5 | LIMITATIONS, NEEDS AREAS, AND NEXT STEPS

The practicality of instrument use and implementation in primary or specialty care offices is an ongoing challenge in dementia risk assessment and care. Lack of familiarity with instruments may result in difficulties with interpretation or serve as barriers to use or uptake. While the recommendations include assessments of cognition, behavior, and function, using both patient and informant sources, the reality of coordinating this is a limitation. However, the current best evidence does support this approach. Clinicians may consider splitting up assessments over several visits (especially in primary care) or incorporating telehealth to obtain informant input. The guidelines also may not necessarily account for the preferences of patient and informant, and the risk of assessment burden or burnout is a possibility.

Development of virtual assessments and tools will be required in the future as many older persons may not be able to travel to specialized centers or even family physicians due to weather; lack of transportation; lack of funds; and now, a worldwide pandemic. Furthermore, many older adults may prefer to stay in their own home for assessments—as it is comfortable, familiar, and possibly less anxiety provoking. This is, of course, predicated on their ability to use technology or having the adequate Internet bandwidth for appropriate remote assessments. As the field further evolves, potentially through identification of even earlier stages of disease, the guidelines will also evolve to stay in-step of knowledge advancement and patient care. While AD is the most common dementia, additional practical assessments will be required to identify other non-AD dementias.

6 | CONCLUSION

CCCDTD5 is an update of the 2008 guidelines on dementia screening, case finding, and assessment to provide current evidence-based approaches for dementia care. Within Canada, individual jurisdictions and access to care vary, and these recommendations are intended as guidelines for clinicians to implement in their practices based on available resources. The recommendations may also be useful to professional groups in other countries, taking into account local culture and resources.

TABLE 9 Canadian Consensus Conference on Diagnosis and Treatment of Dementia 5 (CCCDTD5) recommendations for tracking response to treatment and change over time

Recommendation	Grade
1. Tracking response to treatment and change over time should be individualized, and requires a multi-dimensional approach. It should not rely on a single tool or clinical domain and requires caregiver or reliable informant input. Clinical response should be based on the assessment of the following clinical domains: cognition, functional autonomy, behavior, as well as caregiver burden. The frequency of clinical visits depends on the individual patients and circumstances but typically varies between 6 to 12 months. Patients with behavioral symptoms of dementia may need more frequent reassessment (3 to 6 months). Not all domains need to be assessed at every visit, but all domains must be evaluated at least annually (Table 7).	1C
2. The commonly used scales in clinical trials of dementia such as the ADAS-Cog and the SIB are not familiar to most clinicians and are not recommended for use in clinical practice (1C). Based on available evidence to date, Folstein's MMSE is recommended as one of the primary tools for tracking cognitive response and change overtime (1A) as It has been used in several clinical trials of ChEI, and is familiar to primary care physicians, but it may be insensitive for detecting early cognitive loss. Alternate tools including the sMMSE, 3MS, MOCA, RUDAS, or CDT, etc. can be reasonable options for follow-up. However, they have not been regularly used in clinical trials and their response and sensitivity to treatment is not readily available (1C). Longitudinal assessment with certain scales such as the MMSE and the MOCA seems to be more meaningful than timepoint evaluations. In specialty clinics, more detailed assessments may be considered, depending on site, familiarity, availability, and preference.	1C 1A 1C
3. Assessment of performance on Instrumental Activities of Daily Living (IADLs) and Activities of Daily Living (ADLs) is integral in the follow-up of treated patients. The commonly used scales in clinical trials of dementia such as the ADCS-ADL and the PDS are not familiar to most clinicians and are not recommended for use in clinical practice. Functional assessment can be done with validated and more familiar tools including the DAD, FAST, FAQ, OARS, Barthel, etc. In specialty clinics, more detailed assessments may be considered, depending on site, familiarity, availability, and preference.	1C
4. Commonly used scales for assessment of behavior in clinical trials of dementia such as the BEHAVE-AD and the NPI are not familiar to many clinicians and are not recommended for use in clinical practice. Assessment of behavior can be done with validated, familiar, and simpler tools including the NPI-Q, GDS (although less sensitive to depressive symptoms with progression of the disease), CSDD, PHQ-9, etc. In specialty clinics, more detailed assessments may be considered, depending on site, familiarity, availability, and preference.	1C
5. Commonly used scales for global assessment in clinical trials of dementia such as the CIBIC-Plus, ADCS-CGIC, or CDR are not familiar to most clinicians and are not recommended for use in clinical practice. Global assessment can be done with validated and simple tools which integrate input from the caregiver such as the IQCODE, HABC-Monitor, etc. In specialty clinics, more detailed assessments may be considered, depending on site, familiarity, availability, and preference.	1C
6. Caregiver burden is a major determinant of hospitalization and nursing home placement. It should be regularly assessed in the follow-up of patients with dementia. This can be done with structured scales such as the Zarit Burden Interview, etc.	1C

Abbreviations: 3MS, Modified Mini-Mental State Examination; ADAS-Cog, Alzheimer's Disease Assessment Scale-Cognitive; ADCS-ADL, Alzheimer's Disease Cooperative Study-Activities of Daily Living; ADCS-CGIC, Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change Scale; BEHAVE-AD, Behavioral Pathology in Alzheimer's Disease; CDR, Clinical Dementia Rating; CDT, Clock Drawing Test; CIBIC-Plus, Clinician's Interview-Based Impression of Change Plus Caregiver Input; CSDD, Cornell Scale for Depression in Dementia; DAD, Disability Assessment for Dementia; FAQ, Functional Activities Questionnaire; FAST, Functional Assessment Staging; GDS, Global Deterioration Scale; HABC-Monitor, Healthy Aging Brain Care Monitor; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NPI-Q, The Neuropsychiatric Inventory Questionnaire; PDS, Progressive Deterioration Scale; PHQ-9, Patient Health Questionnaire-9; OARS, Observved Affect Rating Scale; RUDAS, Rowland Universal Dementia Assessment; SIB, Severe Impairment Battery; sMMSE, Standardized Mini-Mental State Examination.

REFERENCES

1. Ismail Z, Black S, Camicioli R, et al. Recommendations of the 5th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia. *Alzheimer's Dementia*. 2020;in press.

2. Association CM. Assessing dementia: the Canadian consensus. Organizing committee, Canadian Consensus Conference on the assessment of dementia. *CMAJ*. 1991;144(7):851-853.

3. Folstein MF, Folstein SE, 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.

4. Patterson C, Gauthier S, Bergman H, et al. The recognition, assessment and management of dementing disorders: conclusions from the Canadian Consensus Conference on dementia. *CMAJ*. 1999; 160:S1.

5. Pfeffer R, Kurosaki T, Harrah C, Chance J, Filos S. Measurement of functional activities in older adults in the community. *J Gerontol*. 1982;37:323-9.

6. Chertkow H. Diagnosis and treatment of dementia: introduction. Introducing a series based on the third Canadian Consensus Conference on the Diagnosis and Treatment of Dementia. *CMAJ*. 2008;178:316-321.

7. Chertkow H, Massoud F, Nasreddine Z, et al. Diagnosis and treatment of dementia: 3. Mild cognitive impairment and cognitive impairment without dementia. *CMAJ*. 2008;178:1273-1285.

8. Nasreddine ZS, Phillips NA, Bédirian V, et al. The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53:695-699.

9. Feldman HH, Jacova C, Robillard A, et al. Diagnosis and treatment of dementia: 2. diagnosis. *CMAJ*. 2008;178:825-836.

10. Hogan DB, Bailey P, Black S, et al. Diagnosis and treatment of dementia: 5. nonpharmacologic and pharmacologic therapy for mild to moderate dementia. *CMAJ*. 2008;179:1019-1026.

11. 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.

12. Herrmann N, Gauthier S. Diagnosis and treatment of dementia: 6. management of severe Alzheimer disease. *CMAJ*. 2008;179:1279-1287.

13. Gauthier S, Patterson C, Chertkow H, et al. Recommendations of the 4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDTD4). *Can Geriatr J*. 2012;15:120.

14. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336:924-926.

15. Lang L, Clifford A, Wei L, et al. Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. *BMJ Open*. 2017;7:e011146.

16. Organization WH. *Dementia a Public Health Priority*. Geneva, Switzerland: World Health Organization; 2012.

17. Fowler NR, Perkins AJ, Gao S, Sachs GA, Boustani MA. Risks and benefits of screening for dementia in primary care: the Indiana university cognitive health outcomes investigation of the comparative effectiveness of dementia screening (IU CHOICE) trial. *J Am Geriatr Soc*. 2020;68:535-543.

18. Moyer VA. Screening for cognitive impairment in older adults: US preventive services task force recommendation statement. *Ann Intern Med*. 2014;160:791-797.

19. Owens DK, Davidson KW, Krist AH, et al. Screening for cognitive impairment in older adults: US preventive services task force recommendation statement. *JAMA*. 2020;323:757-763.

20. Pottie K, Rahal R, Jaramillo A, et al. Recommendations on screening for cognitive impairment in older adults. *CMAJ*. 2016;188:37-46.

21. Lanctot KL, Herrmann N, Yau KK, et al. Efficacy and safety of cholinesterase inhibitors in Alzheimer's disease: a meta-analysis. *CMAJ*. 2003;169:557-564.

22. Collette C, Robitaille G. Detection and diagnosis of Alzheimer's Disease and other neuro cognitive disorders. *INESSS Express*. 2015:1-101.

23. Mitchell AJ, Malladi S. Screening and case finding tools for the detection of dementia. Part I: evidence-based meta-analysis of multidomain tests. *Am J Geriatr Psychiatry*. 2010;18:759-782.

24. Chan QL, Shaik MA, Xu J, Xu X, Chen CL, Dong Y. The combined utility of a brief functional measure and performance-based screening test for case finding of cognitive impairment in primary healthcare. *J Am Med Dir Assoc*. 2016;17(372) e9-e11.

25. Borson S SJ, Chen P, Ganguli M. The Mini-Cog as a screen for dementia: validation in a population-based sample. *J Am Geriatr Soc*. 2003;51:1451-1454.

26. Buschke H, Kuslansky G, Katz M, et al. Screening for dementia with the memory impairment screen. *Neurology*. 1999;52: 231-238.

27. Shulman KI. Clock-drawing: is it the ideal cognitive screening test?. *Int J Geriatr Psychiatry*. 2000;15:548-561.

28. 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.

29. Milian M, Leiherr AM, Straten G, Muller S, Leyhe T, Eschweiler GW. The Mini-Cog versus the Mini-Mental State Examination and the clock drawing test in daily clinical practice: screening value in a German memory clinic. *Int Psychogeriatr*. 2012;24:766-774.

30. Lin JS OCE, Rossom RC, et al. *Screening for Cognitive Impairment in Older Adults: An Evidence Update for the U.S. Preventive Services Task Force*. Rockville, MD: Agency for Healthcare Research and Quality (US); 2013.

31. Teng EL, Chui HC. The Modified Mini-Mental State (3MS) examination. *J Clin Psychiatry*. 1987;48:314-318.

32. Storey JE, Rowland JT, Basic D, Conforti DA, Dickson HG. The Rowland Universal Dementia Assessment Scale (RUDAS): a multicultural cognitive assessment scale. *Int Psychogeriatr*. 2004;16:13-31.

33. Holsinger T, Plassman BL, Stechuchak KM, Burke JR, Coffman CJ, Williams JW, Jr. Screening for cognitive impairment: comparing the performance of four instruments in primary care. *J Am Geriatr Soc*. 2012;60:1027-1036.

34. Bernier PJ, Gourdeau C, Carmichael P-H, et al. Validation and diagnostic accuracy of predictive curves for age-associated longitudinal cognitive decline in older adults. *CMAJ*. 2017;189:E1472-E1480.

35. Galvin J, Roe C, Powlishta K, et al. The AD8 A brief informant interview to detect dementia. *Neurology*. 2005;65:559-564.

36. Jorm A, Scott R, Cullen J, MacKinnon A. Performance of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) as a screening test for dementia. *Psychological Med*. 1991;21:785-90.

37. 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;53:471-81.

38. Ismail Z, Aguera-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.

39. Kroenke K, Spitzer RL. The PHQ-9: a new depression diagnostic and severity measure. *Psychiatr Ann*. 2002;32:1-7.

40. Creese B, Griffiths A, Brooker H, et al. Profile of Mild behavioral impairment and factor structure of the mild behavioral impairment checklist in cognitively normal older adults. Int Psychogeriatr. *Int Psychogeriatr*. 2020;32(6):705-717.

41. Costa PT Jr, Williams TF, Somerfield MR, Albert MS, Nutters NM, Folstein MF, et al. Clinical Practice Guideline no. 19. Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research; 1996. Recognition and Initial Assessment of Alzheimer's Disease and Related Dementias. AHCPR Publication no. 97-0702.

42. Sevush S, Leve N. Denial of memory deficit in Alzheimer's disease. *Am J Psychiatry*. 1993;150:748-751.

43. Barrett AM, Eslinger PJ, Ballentine NH, Heilman KM. Unawareness of cognitive deficit (cognitive anosognosia) in probable AD and control subjects. *Neurology*. 2005;64:693-699.

44. Hardy RM, Oyebode JR, Clare L. Measuring awareness in people with mild to moderate Alzheimer's disease: development of the memory awareness rating scale—adjusted. *Neuropsychol Rehabil*. 2006;16:178-193.

45. Tabert MH, Albert SM, Borukhova-Milov L, et al. Functional deficits in patients with mild cognitive impairment: prediction of AD. *Neurology*. 2002;58:758-764.

46. Briggs R, O'Neill D. The informant history: a neglected aspect of clinical education and practice. *QJM*. 2016;109:301-302.

47. 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 Alzheimers Dis* 2010;22(3):1015-1021.

48. Jorm AF, Broe GA, Creasey H, et al. Further data on the validity of the informant questionnaire on cognitive decline in the elderly (IQCODE). *Int J Geriatric Psychiatry*. 1996;11:131-139.

49. Farias ST, Mungas D, Reed BR, et al. The measurement of everyday cognition (ECog): scale development and psychometric properties. *Neuropsychology*. 2008;22:531.

50. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9:179-186.

51. 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 Geriatric Psychiatry Neurol*. 2013;26:244-250.

52. Clark CM, Ewbank DC. Performance of the dementia severity rating scale: a caregiver questionnaire for rating severity in Alzheimer disease. *Alzheimer Dis Assoc Disord*. 1996;10:31-39.

53. Galvin JE. The Quick Dementia Rating System (QDRS): a rapid dementia staging tool. *Alzheimer's Dementia*. 2015;1:249-259.

54. 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

55. Creese B, Brooker H, Ismail Z, et al. Mild Behavioral impairment as a marker of cognitive decline in cognitively normal older adults. *Am J Geriatr Psychiatry*. 2019;27:823-834.

56. Mallo SC, Ismail Z, Pereiro AX, et al. Assessing mild behavioral impairment with the mild behavioral impairment checklist in people with subjective cognitive decline. *Int Psychogeriatr*. 2019;31:231-9.

57. 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 Alzheimes Dis*. 2018;66:83-95.

58. Barberger-Gateau P, Fabrigoule C, Helmer C, Rouch I, Dartigues JF. Functional impairment in instrumental activities of daily living: an early clinical sign of dementia? *J Am Geriatr Soc*. 1999;47:456-462.

59. 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. *Cochrane Database Syst Rev*. 2016;2016(1):CD011145.

60. Arevalo-Rodriguez I, Smailagic N, i Figuls MR, et al. Mini-Mental State Examination (MMSE) for the detection of Alzheimer's disease and other dementias in people with mild cognitive impairment (MCI). *Cochrane Database Syst Rev*. 2015;2015(3):CD010783.

61. Reiner K, Eichler T, Hertel J, Hoffmann W, Thyrian JR. The clock drawing test: a reasonable instrument to assess probable dementia in primary care? *Curr Alzheimer Res*. 2018;15:38-43.

62. Mioshi E, Dawson K, Mitchell J, Arnold R, Hodges JR. The Addenbrooke's Cognitive Examination Revised (ACE-R): a brief cognitive test battery for dementia screening. *Int J Geriatr Psychiatry*. 2006;21:1078-1085.

63. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology*. 1993;43:2412-2414.

64. Podhorna J, Krahnke T, Shear M, Harrison JE. Alzheimer's disease assessment scale—cognitive subscale variants in mild cognitive impairment and mild Alzheimer's disease: change over time and the effect of enrichment strategies. *Alzheimer's Res Ther*. 2016;8:8.

65. Huppert FA, Brayne C, Gill C, Paykel E, Beardsall L. CAMCOG—a concise neuropsychological test to assist dementia diagnosis: sociodemographic determinants in an elderly population sample. *Br J Clin Psychol*. 1995;34:529-541.

66. Kalbe E, Kessler J, Calabrese P, et al. DemTect: a new, sensitive cognitive screening test to support the diagnosis of mild cognitive impairment and early dementia. *Int J Geriatr Psychiatry*. 2004;19:136-143.

67. Hall K, Hendrie HC, Brittain HM, et al. The development of a dementia screening interview in two distinct languages. *Int. J. Methods Psychiatr. Res.* 1993;3:128.

68. Matias-Guiu JA, Valles-Salgado M, Rognoni T, Hamre-Gil F, Moreno-Ramos T, Matías-Guiu J. Comparative diagnostic accuracy of the ACE-III, MIS, MMSE, MoCA, and RUDAS for screening of Alzheimer disease. *Dement Geriatr Cogn Disord*. 2017;43: 237-246.

69. O'caoimh R, Gao Y, Gallagher PF, Eustace J, McGlade C, Molloy DW. Which part of the Quick mild cognitive impairment screen (Q mci) discriminates between normal cognition, mild cognitive impairment and dementia? *Age Ageing*. 2013;42:324-330.

70. O'Caoimh R, Timmons S, Molloy DW. Screening for mild cognitive impairment: comparison of "MCI specific" screening instruments. *J Alzheimes Dis*. 2016;51:619-629.

71. Freedman M, Leach L, Tartaglia MC, et al. The Toronto Cognitive Assessment (TorCA): normative data and validation to detect amnestic mild cognitive impairment. *Alzheimer's Res Ther*. 2018;10: 65.

72. Breton A, Casey D, Arnaoutoglou NA. Cognitive tests for the detection of mild cognitive impairment (MCI), the prodromal stage of dementia: meta-analysis of diagnostic accuracy studies. *Int J Geriatr Psychiatry*. 2019;34:233-242.

73. Laforce Jr R, Sellami L, Bergeron D, et al. Validation of the Dépistage Cognitif de Québec: a new cognitive screening tool for atypical dementias. *Arch Clin Neuropsychol*. 2018;33:57-65.

74. Sellami L, Meilleur-Durand S, Chouinard A-M, et al. The Dépistage Cognitif de Québec: a new clinician's tool for early recognition of atypical dementia. *Dement Geriatr Cogn Disord*. 2018;46: 310-321.

75. Myers CA, Keller JN, Allen HR, et al. Reliability and validity of a novel internet-based battery to assess mood and cognitive function in the elderly. *J Alzheimes Dis*. 2016;54:1359-1364.

76. Sewell MC, Luo X, Neugroschl J, Sano M. Detection of mild cognitive impairment and early stage dementia with an audio-recorded cognitive scale. *Int Psychogeriatr*. 2013;25:1325-1333.

77. Scanlon L, O'Shea E, O'Caoimh R, Timmons S. Usability and validity of a battery of computerised cognitive screening tests for detecting cognitive impairment. *Gerontology*. 2016;62:247-252.

78. Larouche E, Tremblay M-P, Potvin O, et al. Normative data for the Montreal cognitive Assessment in middle-aged and elderly Quebec-French people. *Arch Clin Neuropsychol*. 2016;31:819-826.

79. Jessen F, Amariglio RE, Van Boxtel M, et al. A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimers Dement*. 2014;10:844-852.

80. Amariglio RE, Becker JA, Carmasin J, et al. Subjective cognitive complaints and amyloid burden in cognitively normal older individuals. *Neuropsychologia*. 2012;50:2880-2886.

81. Mitchell A, Beaumont H, Ferguson D, Yadegarfar M, Stubbs B. Risk of dementia and mild cognitive impairment in older people with

subjective memory complaints: meta-analysis. *Acta Psychiatr Scand.* 2014;130:439-451.

82. Slot RE, Verfaillie SC, Overbeek JM, et al. Subjective Cognitive Impairment Cohort (SCIENCe): study design and first results. *Alzheimer's Res Ther.* 2018;10:76.

83. Cacciamani F, Tandetnik C, Gagliardi G, et al. Low cognitive awareness, but not complaint, is a good marker of preclinical Alzheimer's disease. *J Alzheimes Dis.* 2017;59:753-762.

84. Crumley JJ, Stetler CA, Horhota M. Examining the relationship between subjective and objective memory performance in older adults: a meta-analysis. *Psychol Aging.* 2014;29:250.

85. Agüera-Ortiz L, Lyketsos C, Ismail Z. Comment on "personality changes during the transition from cognitive health to mild cognitive impairment". *J Am Geriatr Soc.* 2019;67(1):190-191.

86. Caselli RJ, Langlais BT, Dueck AC, et al. Personality changes during the transition from cognitive health to mild cognitive impairment. *J Am Geriatr Soc.* 2018;66:671-678.

87. Molinuevo JL, Rabin LA, Amariglio R, et al. Implementation of subjective cognitive decline criteria in research studies. *Alzheimers Dement.* 2017;13:296-311.

88. Balash Y, Mordechovich M, Shabtai H, Giladi N, Gurevich T, Korczyn A. Subjective memory complaints in elders: depression, anxiety, or cognitive decline? *Acta Neurol Scand.* 2013;127:344-350.

89. Taragano FE, Allegri RF, Heisecke SL, et al. Risk of conversion to dementia in a mild behavioral impairment group compared to a psychiatric group and to a mild cognitive impairment group. *J Alzheimes Dis.* 2018;62:227-238.

90. Cano J, Chan V, Kan CN, et al. Mild behavioral impairment: prevalence in clinical setting and cognitive correlates. *Alzheimer's Dementia.* 2018;14:P639-P40.

91. Geda YE, Roberts RO, Mielke MM, et al. Baseline neuropsychiatric symptoms and the risk of incident mild cognitive impairment: a Population-Based Study. *Am J Psychiatry.* 2014;171:572-581.

92. Matsuoka T, Ismail Z, Narumoto J. Prevalence of mild behavioral impairment and risk of dementia in a psychiatric outpatient clinic. *J Alzheimes Dis.* 2019;70:505-513.

93. Taragano FE, Allegri RF, Krupitzki H, Sarasola D, Serrano C, Lyketsos C. Mild behavioral impairment. *J Clin Psychiatry.* 2009;70:584-592.

94. Banks SJ, Raman R, He F, Salmon DP, Ferris S, Aisen P, et al. The Alzheimer's disease cooperative study prevention instrument project: longitudinal outcome of behavioral measures as predictors of cognitive decline. *Dement Geriatr Cog Dis Extra.* 2014;4:509-516.

95. Masters MC, Morris JC, Roe CM. "Noncognitive" symptoms of early Alzheimer disease a longitudinal analysis. *Neurology.* 2015;84:1-6.

96. Wise EA, Rosenberg PB, Lyketsos CG, Leoutsakos J-M. Time course of neuropsychiatric symptoms and cognitive diagnosis in National Alzheimer's Coordinating Centers volunteers. *Alzheimer's Dementia.* 2019;11:333-339.

97. Donovan NJ, Amariglio RE, Zoller AS, et al. Subjective cognitive concerns and neuropsychiatric predictors of progression to the early clinical stages of Alzheimer disease. *Am J Geriatr Psychiatry.* 2014;22:1642-1651.

98. Ismail Z, Gatchel J, Bateman DR, et al. Affective and emotional dysregulation as pre-dementia risk markers: exploring the mild behavioral impairment symptoms of depression, anxiety, irritability, and euphoria. *Int Psychogeriatr.* 2018;30:185-196.

99. 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.

100. Ismail Z, McGirr A, Gill S, Hu S, Forkert ND, Smith EE. Mild behavioral impairment and subjective cognitive decline predict mild cognitive impairment. *medRxiv.* 2020;2020:20112284.

101. Sheikh J, Yesavage J. Geriatric Depression Scale (GDS): recent findings and development of a shorter version. In: Brink T, ed. *Clinical Gerontology: A Guide to Assessment and Intervention.* New York: Howarth Press; 1986.

102. Löwe B, Decker O, Müller S, et al. Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. *Med Care.* 2008;46:266-274.

103. Rami L, Mollica MA, García-Sanchez C, et al. The subjective cognitive decline questionnaire (SCD-Q): a validation study. *J Alzheimes Dis.* 2014;41:453-466.

104. Sullivan J, Edgley K, Dehoux E. A survey of multiple sclerosis. Part I: perceived cognitive problems and compensatory strategy used. *Can J Rehabil.* 1990;4:99-105.

105. WHO. Risk reduction of cognitive decline and dementia: WHO guidelines. *Risk Reduction of Cognitive Decline and Dementia.* Geneva, Switzerland: WHO Guidelines; 2019.

106. Panisset M, Roudier M, Saxton J, Boiler F. Severe impairment battery: a neuropsychological test for severely demented patients. *Arch Neurol.* 1994;51:41-45.

107. Galasko D, Bennett D, Sano M, et al. An inventory to assess activities of daily living for clinical trials in Alzheimer's disease. *Alzheimer Dis Assoc Disord.* 1997;11(Suppl 2):S33-S39.

108. DeJong R, Osterlund O, Roy G. Measurement of quality-of-life changes in patients with Alzheimer's disease. *Clin Therapeutics.* 1989;11:545-554.

109. Reisberg B, Auer SR, Monteiro IM. Behavioral pathology in Alzheimer's disease (BEHAVE-AD) rating scale. *Int Psychogeriatr.* 1997;8:301-308.

110. Zarit SH, Reever KE, Bach-Peterson J. Relatives of the impaired elderly: correlates of feelings of burden. *Gerontologist.* 1980;20:649-655.

111. Knopman DS, Knapp MJ, Gracon SI, Davis CS. The Clinician Interview-Based Impression (CIBI): A clinician's global change rating scale in Alzheimer's disease. *Neurology.* 1994;44:2315

112. Sclan SG, Reisberg B. Functional assessment staging (FAST) in Alzheimer's disease: reliability, validity, and ordinality. *Int Psychogeriatr.* 1992;4:55-69.

113. Fillenbaum GG, Smyer MA. The development, validity, and reliability of the OARS multidimensional functional assessment questionnaire. *J Gerontol.* 1981;36:428-434.

114. Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index: a simple index of independence useful in scoring improvement in the rehabilitation of the chronically ill. *MD State Med J.* 1965;14:61-65.

115. Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell scale for depression in dementia. *Biol Psychiatry.* 1988;23:271-284.

116. Monahan PO, Alder CA, Khan BA, Stump T, Boustani MA. The Healthy Aging Brain Care (HABC) monitor: validation of the patient self-report version of the clinical tool designed to measure and monitor cognitive, functional, and psychological health. *Clin Interv Aging.* 2014;9:2123.