Perspective

Recommendations of the 5th Canadian Consensus Conference on the diagnosis and treatment of dementia

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Abstract
Since 1989, four Canadian Consensus Conferences on the Diagnosis and Treatment of Dementia (CCCDTD) have provided evidence-based dementia guidelines for Canadian clinicians and researchers. We present the results of the 5th CCCDTD, which convened in October 2019, to address topics chosen by the steering committee to reflect advances in the field, and build on previous guidelines. Topics included: (1) utility of the National Institute on Aging research framework for clinical Alzheimer’s disease (AD) diagnosis; (2) updating diagnostic criteria for vascular cognitive impairment, and its management; (3) dementia case finding and detection; (4) neuroimaging and fluid biomarkers in diagnosis; (5) use of non-cognitive markers of dementia for better dementia detection; (6) risk reduction/prevention; (7) psychosocial and non-pharmacological interventions; and (8) deprescription of medications used to treat dementia. We hope the guidelines are useful for clinicians, researchers, policy makers, and the lay public, to inform a current and evidence-based approach to dementia.

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1 | INTRODUCTION

Since 1989, four Canadian Consensus Conferences on the Diagnosis and Treatment of Dementia (CCCDTD) have led to evidence-based recommendations on the diagnosis and treatment of Alzheimer’s disease (AD) and related dementias.1–4 The 5th CCCDTD convened in October 2019 in Quebec City, in conjunction with the Canadian Conference on Dementia in order to provide new guidelines with novel information relevant to the field. Topics included: (1) Utility of the National Institute on Aging (NIA) research framework for clinical AD diagnosis; (2) updating diagnostic criteria for vascular cognitive impairment (VCI) and its management; (3) dementia case finding and detection; (4) use of neuroimaging and fluid biomarkers in diagnosis; (5) use of non-cognitive markers of dementia for better dementia detection; (6) risk reduction/prevention; (7) psychosocial and non-pharmacological interventions; and (8) deprescription of medications used to treat dementia.

2 | METHODS

The methodology was guided by the AGREE II collaboration5 of which 20 of the 23 criteria were met. The steering committee chose the topics for CCCDTD5 based on a needs assessment and advances in the field. Working groups were formed, chosen by steering committee members. Overall representation was required for neurology, psychiatry, geriatric medicine, primary care, and experienced researchers in the field. Literature searches were tailored to the group needs depending on whether the recommendations were updates or de novo topics (described below).

We attempted to follow, where possible, the GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) system in keeping with current recommendations for the conduct of consensus conferences.6 A semi-structured consensus building methodology was used, based on the Delphi process.7,8 Each working group internally generated recommendations, which were then posted to a password-protected site, along with background documentation and literature search, for viewing and voting by a panel of >50 Canadian experts from various backgrounds. Recommendations were endorsed or rejected, with comment boxes for participant feedback. Consistent with previous conferences, the a priori threshold for acceptance of recommendations was set at 80% endorsement, with recommendations obtaining between 60% and 80% endorsement requiring revision and re-voting at an in-person meeting with two delegates per working group. Recommendations obtaining <60% endorsement were dropped.

Organizations relevant to the care of people with dementia representing industry, government, international experts, and other dementia guideline organizations had been invited to appoint non-voting delegates as observers. Online voting closed 3 days before the conference assembly, which was held in Quebec on October 3, 2019. At the conference each topic was briefly summarized along with the results of the online voting. Recommendations requiring revision were discussed in detail followed by an anonymous vote. The same ≥80% threshold was required for revised recommendations. All endorsed recommendations are listed in the tables of this article, followed by GRADE of evidence and percentage endorsement in initial vote (and subsequent vote where relevant).

3 | RECOMMENDATIONS

This summary paper lists the recommendations that reached consensus. Subsequent articles written by each working group will expand on the background work and describe in more depth the clinical impact of these recommendations.

3.1 | NIA research framework for AD diagnosis

The NIA-AA Research Framework is proposing a biological definition of AD, intended for observational and interventional research, not routine clinical care.9 It is proposed that the diagnosis of AD is not based on the clinical consequences of the disease (ie, symptoms/signs), but on biomarkers of amyloid beta (Aβ) deposition, pathologic tau, and neurodegeneration (ATN). The authors did emphasize that it was premature to use this research framework in general medical practice (Table 1).

3.2 | Diagnosis and treatment of VCI

VCI is the second most important contributor to cognitive decline and dementia, after AD. Although recent VCI diagnostic criteria have not been validated neuropathologically in large samples, they do exhibit greater reliability than older criteria.10 Here we provide recommendations for neuroimaging,11 prevention,12 and management of stroke and stroke risk factors including hypertension,13,14 and pharmacological management of VCI (Table 2).15

3.3 | Dementia case finding and detection

The goal was to use the most current evidence to provide practical approaches to clinical issues with little clinical guidance (eg, how to approach subjective cognitive decline [SCD]), describe higher risk groups warranting further investigation and workup, and provide algorithmic approaches to assessments using all sources of information. We updated previous recommendations from CCCDTD3 on case detection tools,3,19,20 and also incorporated the 2015 Canadian Institut National d’Excellence en Santé et Services Sociaux (INESS) document on detection and diagnosis of AD and other neurocognitive disorders.21 There was a clear emphasis on obtaining information from a reliable informant, in the multiple domains of cognition, behavior, and function, to address a broader spectrum of dementia phenotypes encompassing preclinical, prodromal, and dementia proper (Table 3).
TABLE 1  National Institute on Aging research framework for Alzheimer’s disease diagnosis

1. We recommend the adoption of the criteria for the biological (ATN) definition of Alzheimer’s disease proposed by the NIA-AA working group in 2018 only for observational and interventional research. 1B (94%)

2. We recommend the addition to this biological definition of other pathological factors such as vascular, inflammatory, synuclein, and TDP-43 as soon as there are validated instruments to reliably measure their levels. 1C (87%)

3. Given that the presence of brain amyloid and/or tau in cognitively normal people is of uncertain significance, we discourage the use of amyloid and tau imaging without memory decline, outside of the research setting. The medical community should be clear in its discussion with patients, the media, and the general population that the presence of brain amyloid and/or tau in normal people is of unclear significance at the present time. 1A (100%)

TABLE 2  Diagnosis and treatment of vascular cognitive impairment

1. Magnetic resonance imaging (MRI) is recommended over computed tomography (CT) for investigating vascular cognitive impairment. 2C (98%)

2. Use of standardized criteria (one of: the Vascular Behavioral and Cognitive Disorders [VAS-COG] Society criteria, Diagnostic and Statistical Manual of Mental Disorders [DSM5], Vascular Impairment of Cognition Classification Consensus Study, or the American Heart Association consensus statement) are recommended for the diagnosis of vascular mild cognitive impairment and vascular dementia. 1C (100%)

3a. Because treatment of hypertension may reduce risk of dementia, clinicians should assess, diagnose, and treat hypertension according to guidelines from Hypertension Canada. 1B (98%)

3b. For patients with cognitive disorders in which a vascular contribution is known or suspected, antihypertensive therapy should be strongly considered for average diastolic blood pressure readings ≥ 90 mmHg and for average systolic blood pressure readings > 140 mmHg. 1B (96%)

3c. In middle-aged and older persons being treated for hypertension who have associated vascular risk factors a systolic BP treatment target of < 120 mmHg may be associated with a decreased risk of developing mild cognitive impairment and should be considered when deciding on the intensity of their therapy. 1C (83%)

4. All patients with cognitive symptoms or impairment should receive guideline-recommended treatments to prevent first-ever or recurrent stroke, as appropriate. 1B (98%)

5a. The use of aspirin is not recommended for patients with MCI or dementia who have brain imaging evidence of covert white matter lesions of presumed vascular origin without history of stroke or brain infarcts. 2C (96%)

5b. The effects of aspirin on cognitive decline in patients with MCI or dementia who have covert brain infarcts detected on neuroimaging without history of stroke has not been defined. The use of aspirin in this setting is reasonable, but the benefit is unclear. 2C (86%)

6. Cholinesterase inhibitors (donepezil, galantamine, rivastigmine) and the N-methyl-D-aspartate (NMDA) receptor antagonist memantine may be considered for the treatment of vascular cognitive impairment in selected patients. 2B (89%)

TABLE 3  Dementia case finding and detection

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

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 (95%)

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) then validated assessments of cognition, activities of daily living, and neuropsychiatric symptoms are indicated (see subsequent sections for suggestions for valid tools). 1A (95%)

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 (98%)

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

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 (95%)

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 (95%)

(Continues)
TABLE 3 (Continued)

3. In persons with elevated risk for cognitive disorders or with medical conditions associated with cognitive disorders such as 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 (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 (93%)

4. The distinction between MCI and dementia is important and is currently made on the basis of clinical 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 (88%)

5. An objective assessment of the patient's cognitive function could be achieved by using rapid psychometric screening tools such as the Memory Impairment Screen (MIS) examination, the Mini-Mental State Examination (MMSE), or the Rowland Universal dementia assessment scale (RUDAS). MMSE remains the most widely used instrument, with high sensitivity and specificity for separating moderate dementia from normal cognition and is recommended in many countries. However, it lacks sensitivity for the diagnosis of mild dementia or MCI. The MoCA is more sensitive to MCI than the MMSE and its use is recommended when mild cognitive impairment is suspected or in cases where there is suspicion of cognitive impairment or concern about the patient's cognitive status, and the MMSE score is in the “normal” range (24+ out of 30). 1B (93%)

6. If more time is allowed, preference should be given to using a more comprehensive psychometric screening tool (the Modified Mini-Mental State Examination, the Mini-Mental State Examination [MMSE]) or the Rowland Universal dementia assessment scale (RUDAS). MMSE remains the most widely used instrument, with high sensitivity and specificity for separating moderate dementia from normal cognition and is recommended in many countries. However, it lacks sensitivity for the diagnosis of mild dementia or MCI. The MoCA is more sensitive to MCI than the MMSE and its use is recommended when mild cognitive impairment is suspected or in cases where there is suspicion of cognitive impairment or concern about the patient's cognitive status, and the MMSE score is in the “normal” range (24+ out of 30). 1B (93%)

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 (80%)

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 Ascertain Dementia 8 (AD-8) questionnaire or the Informant Questionnaire on cognitive decline in the elderly (IQCODE) is recommended. 1B (93%)

9. Combining cognitive tests with functional screens and informant reports may improve case-finding in people with cognitive difficulties. 1A (95%)

10. Rapid screening of functional autonomy should be completed by an objective assessment with the patient and a family member using the Pfeffer Functional Activities Questionnaire (FAQ) or the Disability Assessment for Dementia (DAD). 1C (89%)

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 short version of the Neuropsychiatric Inventory (NPI-Q), Mild Behavioural Impairment Checklist (MBI-C) or if a mood change has been observed with the Patient Health Questionnaire-9 (PHQ). 1A (93%)

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

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 (91%)

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 (93%)

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 (86%)

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, Quick Dementia Rating System [QDRS]); measure informant's report on functional changes combined with cognitive assessment as an alternative (eg, FAQ, Lawton-Brody IADL, 4-item IADL scale [4-IADL], Amsterdam IADL questionnaire [A-IADL-Q]); measure informant's report on behavioral changes (eg, NPI-Q, MBI-C). 1B (86%)

What instruments can be used to get more in-depth information to diagnose MCI or dementia?

In addition to neuropsychological testing (if available), we make the following recommendations with regard to the instruments available for more in-depth cognitive evaluation of MCI and dementia:

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 (100%)

2. Cognitive screening tools exist specifically for the early identification of MCI (MoCA, TorCA). Among them, the MoCA offers strong normative data (1C) while the TorCA has just been recently published (2B). 87%

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 (84%)

4. Innovative new tools exist, similar to growth curves used in pediatrics, to allow longitudinal cognitive evaluation based on serial cognitive assessments. 1C (80%)

(Continues)
TABLE 3 (Continued)

What is the approach to those with cognitive concerns but without objective cognitive changes (i.e., recommendations for subjective cognitive decline [SCD])?

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 (i.e., standard dementia medical workup to identify reversible causes, and psychiatric symptom assessment, with a special emphasis on depressive and anxious symptoms). 1B (93%)

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 (i.e., new onset symptoms vs chronic or longstanding symptoms). GRADE 1B (95%)

3. Use of structured scales for: objective cognition (e.g., MoCA, Clock Drawing Test); subjective cognition (e.g., SCD-Q part 1 [MyCog][46]); informant reported cognition/function (e.g., ECog, Informant Questionnaire on Cognitive Decline in the Elderly [IQCODE], Lawton Instrumental Activities of Daily Living Scale. Perceived Deficits Questionnaire [Pdq],47 SCD-Q part 2 [TheirCog][46]); and behavior (e.g., informant report [MBI-C, NPI-Q] and self [GDS,48 PHQ9, GAD7][49]) is recommended. 1B (95%)

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 (89%)

5. For patients with a positive corroborative history, annual follow-ups are recommended. 1B (91%)

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 (86%)

7. Patients with SCD and significant psychiatric symptoms could be referred for psychiatric assessment and/or treatment, depending on the clinician’s expertise. 1B (95%)

8. All patients presenting with SCD should be provided with information on the World Health Organization recommendations for the prevention of dementia.39 1C (98%)

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

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. Not all domains need to be assessed at every visit, but all domains must be evaluated at least annually. 1C (95%)

2. The commonly used scales in clinical trials of dementia such as the Alzheimer’s Disease Assessment Scale–Cognition (ADAS–Cog) and the Severe Impairment Battery (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 Mini-Mental Status Examination (MMSE) is recommended as one of the primary tools for tracking cognitive response and change over time (1A) as it has been used in several clinical trials of cholinesterase inhibitors (ChEI), and is familiar to primary care physicians, but it may be insensitive for detecting early cognitive loss. Alternate tools including the standardized MMSE, the Modified MMSE (3MS), the Montreal Cognitive Assessment (MOCA), the Rowland Universal Dementia Assessment Scale (RUDAS), or the Clock Drawing Test, 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 time point evaluations. In specialty clinics, more detailed assessments may be considered, depending on site, familiarity, availability, and preference. (91%)

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 Alzheimer’s Disease Cooperative Study Activities of Daily Living (ADCS-ADL), and the Progressive Deterioration Scale (PDS) are not familiar to most clinicians and are not recommended for use in clinical practice (1C). Functional assessment can be done with validated and more familiar tools including the Disability Assessment in Dementia (DAD), Functional Assessment Staging Scale (FAST), Functional Activities Questionnaire (FAQ), the Older Americans Resources and Services Multidimensional Functional Assessment (OARS)[33] the Barthel Index Score, etc. (1C). In specialty clinics, more detailed assessments may be considered, depending on site, familiarity, availability, and preference. (95%)

4. Commonly used scales for assessment of behavior in clinical trials of dementia such as the Behavioral Pathology in Alzheimer’s Disease Rating Scale (BEHAVE-AD)[34] and the Neuropsychiatric Inventory (NPI) are not familiar to many clinicians and are not recommended for use in clinical practice (1C). Assessment of behavior can be done with validated, familiar, and simpler tools including the NPI-Q (brief version of the NPI), the Geriatric Depression Scale (GDS; although less sensitive to depressive symptoms with progression of the disease), the Cornell Scale for Depression in Dementia, the Patient Health Questionnaire (PHQ-9) etc. (1C). In specialty clinics, more detailed assessments may be considered, depending on site, familiarity, availability, and preference. (95%)

5. Commonly used scales for global assessment in clinical trials of dementia such as the Clinician’s Interview-Based Impression of Change Plus Caregiver Input (CIBIC-Plus).[35] The Alzheimer’s Disease Cooperative Study–Clinical Global Impression of Change (ADCS–CGIC)[36] or the Clinical Dementia Rating scale (CDR) are not familiar to most clinicians and are not recommended for use in clinical practice (1C). Global assessment can be done with validated and simple tools that integrate input from the caregiver such as the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), the HABC-Monitor, etc. (1C). In specialty clinics, more detailed assessments may be considered, depending on site, familiarity, availability, and preference. (98%)

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 (91%)

7. 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.
### TABLE 4  Use of neuroimaging and fluid biomarkers

| Structural Imaging |
|--------------------|
| 1. Even in older subjects, anatomical neuroimaging is recommended in most situations, using the following list of indications: onset of cognitive signs/symptoms within the past 2 years, regardless of the rate of progression; unexpected and unexplained decline in cognition and/or functional status in a patient already known to have dementia; recent and significant head trauma; unexplained neurological manifestations (new onset severe headache, seizures, Babinski sign, etc.), at onset or during evolution (this also includes gait disturbances); history of cancer, in particular if “at risk” for brain metastases; subject at risk for intracranial bleeding; symptoms compatible with normal pressure hydrocephalus; significant vascular risk factors. 1C (76%; 93%) |
| 2. Magnetic resonance imaging (MRI) is recommended over computed tomography (CT), especially given its higher sensitivity to vascular lesions as well as for some subtypes of dementia and rarer conditions (2C). (87%) If available, and in the absence of contraindications, 3T MRI should be favoured over 1.5 T. (2C) (91%) If MRI is performed, we recommend the use of the following sequences: 3D T1 volumetric sequence (including coronal reformations for the purpose of hippocampal volume assessment), fluid-attenuated inversion recovery (FLAIR), T2 (or if available susceptibility-weighted imaging (SWI)) and diffusion-weighted imaging (DWI). 1C (98%) We recommend against the routine clinical use of advanced MR sequences such as rs-fMRI, MR spectroscopy, diffusion tensor imaging (DTI), and arterial spin labelling (ASL). However, these sequences are promising research tools that can be incorporated in a research setting or if access to advanced expertise is present. 2C (98%) |
| 3. If CT is performed, we recommend a non-contrast CT and coronal reformations are encouraged to better assess hippocampal atrophy. 1C (100%) |
| 4. We recommend the use of semi-quantitative scales for routine interpretation of both MRI and CT scans including: the medial temporal lobe atrophy (MTA) scale for medial temporal involvement, Fazekas scale for white matter changes, and global cortical atrophy (GCA) to qualify global atrophy. 1C (96%) |
| 5. We recommend against the routine clinical use of quantification software pending larger studies demonstrating the added diagnostic value of these tools. Of note, this is a rapidly evolving field and such recommendation could change in the future. 2C (93%) |

| Functional and Ligand-Based Imaging |
|------------------------------------|
| 3a. For a patient with a diagnosis of a cognitive impairment who has undergone the recommended baseline clinical and structural brain imaging evaluation and who has been evaluated by a cognitive disorders specialist but whose underlying pathological process is still unclear, preventing adequate clinical management, an [18F]-FDG PET scan is an effective and accurate tool for differential diagnosis purposes. 1A (88%) |
| 3b. If such a patient cannot be practically referred for a FDG-PET scan, we recommend that a SPECT rCBF study be performed for differential diagnosis purposes. 1B (86%) |
| 4a. As recommended by The Amyloid Imaging Task Force of the Alzheimer’s Association and Society for Nuclear Medicine and Molecular Imaging as well as by The Canadian Consensus Conference on the Use of Amyloid Imaging, ordering PET amyloid imaging tests should be limited to dementia experts. 1A (98%) |
| 4b. Because of cost issues, it is preferable to obtain an [18F]-FDG PET (fluorodeoxyglucose positron emission tomography) scan before proceeding to amyloid imaging. 1A (90%) |
| 4c. Use should follow The Amyloid Imaging Task Force of the Alzheimer’s Association and Society for Nuclear Medicine and Molecular Imaging as well as The Canadian Consensus Conference on the Use of Amyloid Imaging appropriate use criteria. This will result in improved diagnostic classification and management. 1B (93%) |
| 5a. [123I]-Ioflupane and single-photon emission computed tomography (SPECT; DaTscan) can be useful to establish a diagnosis of cognitive impairment linked to Lewy Body Disease in cases where such a diagnosis is suspected but remains unconfirmed after evaluation by a specialist with experience in the evaluation of neurodegenerative disease, thereby preventing adequate clinical management. 2B (93%) |
| 5b. Because of cost issues, it is preferable to obtain an [18F]-FDG PET scan before proceeding to [123I]-Ioflupane SPECT (DaTscan), as this has a high probability of establishing the diagnosis. 1A (93%) |

| Fluid Biomarkers |
|------------------|
| 6. Cerebrospinal fluid (CSF) analysis is not recommended routinely, but it can be considered in dementia patients with diagnostic uncertainty and onset at an early age (<65) to rule out Alzheimer’s disease (AD) pathophysiology. 1C (78%; 100%) |
| 7. CSF analysis can also be considered in dementia patients with diagnostic uncertainty and predominance of language, visuospatial, dysexecutive, or behavioral features to rule out AD pathophysiology. 1C (78%; 100%) |

### TABLE 5  Non-cognitive markers of dementia

| Structural Imaging |
|--------------------|
| 1a. There is strong evidence that slower gait speed is associated with future dementia, in population studies. When gait speed (cut-off gait speed below 0.8m/s) is coupled with cognitive impairment (subjective or objective) the risk is higher. We recommend testing gait speed in clinics in those patients with cognitive complaints/impairments if time/resources are available. 1B (62%, 100%) Note: Protocols on how to assess gait speed with stopwatch are available. Testing takes, on average, 3 minutes to perform. |
| 1b. Dual-task gait impairment (lower speed or high cost) is associated with future incident dementia. In MCI samples, dual-task gait was shown to predict time to progression to dementia. Variability in the delivery of testing protocols is noted. We recommend that dual-task gait test may be used in specialized clinics (memory clinics) to help identify mild cognitive impairment (MCI) older adults at higher risk of progression to dementia if time/resources are available. 2B (60%, 100%) Note: Published protocols on how to assess Dual-Task Gait for dementia risk with just a stopwatch are available. |
TABLE 5  (Continued)

2. The presence of parkinsonism may increase by three times the odds of developing dementia. We recommend routinely assessing parkinsonism as a marker of risk of dementia in memory clinics. 1B (91%)

3a. We recommend that frailty is assessed as a marker of future dementia in primary care and memory clinics. 1B (87%)

3b. We recommend that frailty is included/or adjusted in prediction models of dementia, for clinician researcher settings. 1B (83%)

4a. Older adults presenting with neuropsychiatric symptoms (NPS) should be assessed with respect to the natural history of symptoms. Those with first episode psychiatric symptoms in later life should be assessed for a psychiatric condition, but with a high index of suspicion for a neurocognitive disorder. 1B (96%)

4b. Corroborative information from a reliable informant is recommended. Using a validated informant-rated scale like the Neuropsychiatric Inventory (NPI-Q) or Mild Behavioural Impairment Checklist (MBI-C) will operationalize assessment of NPS, especially in primary care. 1B (91%)

4c. Referral to a memory clinic may be considered for those with later life emergent and sustained NPS, for additional investigation and work up. 2B (94%)

5a. A careful sleep history, including assessment of sleep time, insomnia, daytime sleepiness, napping, and REM sleep behavior disorder, may facilitate identification of pre-clinical dementia, or high risk of developing dementia, and should be included in assessments in both the primary care and specialized memory clinic settings. 1A (91%)

5b. Objective assessment of sleep using actigraphy or polysomnography may facilitate identification of individuals at high risk of developing dementia. Individuals, in whom a careful sleep history, taken in the context of a work up for cognitive impairment or dementia, suggests the possibility of a sleep abnormality, should be referred to a specialized sleep clinic for further assessment. 1C (70%, 91%)

6. There is enough observational evidence that hearing impairment is associated with the development of dementia. We recommend assessing and recording hearing impairment in primary clinics as a dementia risk factor. 1B (87%)

7. There is insufficient evidence to support assessment of vision impairment for dementia risk. However, vision assessment and correction outweigh burden and vision correction could improve cognitive functioning. 1C (87%)

TABLE 6  Risk reduction

Nutrition

1a. We recommend adherence to a Mediterranean diet to decrease the risk of cognitive decline. 1B (91%)

1b. We recommend a high level of consumption of mono- and polyunsaturated fatty acids and a low consumption of saturated fatty acids, to reduce the risk of cognitive decline. 1B (92%)

1c. We recommend increasing fruit and vegetable intake. 1B (88%)

Physical Exercise

2a. We recommend physical activity interventions of at least moderate intensity to improve cognitive outcomes among older adults. 1B (96%)

2b. We recommend aerobic exercise and/or resistance training of at least moderate intensity to improve cognition outcomes among older adults. 1B (94%)

2c. There is promising evidence that dance interventions and mind-body exercise (for example, Tai Chi, Qigong) of moderate dose improve cognitive outcomes among older adults but results from larger, high quality trials are needed. 2B (84%)

3a. We recommend physical activity interventions involving aerobic exercise to improve cognitive outcomes among people with mild cognitive impairment (MCI). 2B (94%)

3b. We recommend aerobic exercise to improve cognitive outcomes among people with MCI. 2B (94%)

3c. There is promising evidence to support resistance training and mind-body exercise (eg, Tai Chi, Qigong) to improve cognitive outcomes among older adults with MCI but results from larger, high quality trials are needed. 2C (83%)

4. We recommend physical activity interventions to reduce the risk of dementia, including Alzheimer’s disease and vascular dementia. 2B (96%)

Hearing

5a. Persons with cognitive complaints, MCI, or dementia (and their care partner, if there is one) should be questioned about symptoms of hearing loss to improve cognitive outcomes and risk reduction. It is recommended that persons are asked if they have any difficulty hearing in their everyday life (rather than asking if they have a hearing loss). 1B (93%)

5b. If symptoms of hearing loss are reported, then hearing loss should be confirmed by audiometry conducted by an audiologist meeting provincial regulations for the practice of audiology. If confirmed, audiologic rehabilitation may be recommended. This rehabilitation may include behavioral counselling and techniques, and may or may not include the recommended use of a hearing aid or other device. 1A (98%)

6. We recommend following the World Health Organization 2019 guidelines for risk reduction of cognitive decline and dementia including: (a) audiological examination and/or otoscopic examination; (b) the review of medications for potential ototoxicity; (c) referral to otolaryngology for persons with chronic otitis media or who fail otoscopy. 1A (93%)
### Table 6 (Continued)

| Sleep |
|-------|
| 7a. A careful sleep history, including assessment of sleep time, and symptoms of sleep apnea, should be included in the assessment of any patient at risk for dementia. Patients in whom sleep apnea is suspected should be referred for polysomnography and/or sleep specialist consultation for consideration of treatment. 1C (96%) |
| 7b. Adults with sleep apnea should be treated with continuous positive airway pressure (CPAP), which may improve cognition and decrease the risk of dementia. 1C (96%) |
| 7c. Avoiding severe (<5 hours) sleep deprivation, and targeting 7-8 hours of sleep per night, may improve cognition and decrease the risk of dementia. 1C (94%) |
| 7d. Although associated with incident cognitive decline and dementia, there is insufficient evidence to recommend treatment of insomnia, long sleep time, daytime napping, sleep fragmentation, circadian irregularity, or abnormal circadian phase with a goal of improving cognition and decreasing the risk of dementia. 3C (90%) |

### Cognitive Training and Stimulation

| 8a. We recommend that when accessible empirically supported individual computer-based and group cognitive training be proposed to people at risk, and those with a diagnosis of mild cognitive impairment or mild dementia. We recommend additional studies to optimize effective delivery of training, and evaluation of their cost effectiveness. No specific program can be endorsed at this time. 1B (83%) |
| 8b. We recommend that individuals be advised to increase or maintain their engagement in cognitively stimulating activities such as cognitively stimulating pastimes, volunteering, and long-life learning. No particular activities can be suggested at this time but data suggest that engaging in a variety of cognitively stimulating activities is preferable. 1C (96%) |

### Social Engagement and Education

| 9a. We recommend attention to social circumstances and supports across the life course, including poverty reduction strategies and opportunities for social engagement. 1B (90%) |
| 9b. We recommend support for educational attainment, particularly in early life (1B) but also for ongoing educational experiences in mid and later life. 1C (98%) |

### Frailty

| 10. We recommend that interventions to manage frailty be used to reduce the overall burden of dementia in older adults. 1B (81%) |

### Medications

| 11a. Exposure to medications known to exhibit highly anticholinergic properties should be minimized in older persons. Alternative medications should be used for specific indications where medications with anticholinergic properties are indicated (eg, depression, neuropathic pain, urge type urinary incontinence). 1B (100%) |
| 11b. Multidimensional health assessment for older adults, including of medication use, with the aim of identifying reversible or modifiable health conditions and rationalizing medication use. 1B (92%) |

### Table 7 Psychosocial interventions

| Individual Level |
|------------------|
| 1. We recommend exercise (group or individual physical exercise) for people living with dementia.98-101 We cannot recommend any specific exercise duration or intensity at this time. 1B (93%) |
| 2. Group cognitive stimulation therapy is an intervention for people with dementia which offers a range of enjoyable activities providing general stimulation for thinking, concentration, and memory usually in a social setting, such as a small group. We recommend considering group cognitive stimulation therapy for people living with mild to moderate dementia.101-104 2B (96%) |
| 3. Psychoeducational interventions for caregivers aim at the development of problem-focused coping strategies while psychosocial interventions address the development of emotion-focused coping strategies. These can include education, counseling, information regarding services, enhancing carer skills to provide care, problem solving, and strategy development. We recommend considering psychosocial and psychoeducational interventions for caregivers of people living with dementia.105-110 2C (96%) |

| Community Level |
|-----------------|
| 4. Dementia friendly organizations/communities are defined as the practice and organization of care/communities that is aware of the impact dementia has on a person’s ability to engage with services and manage their health. It promotes the inclusion of people living with dementia and their caregiver in decisions and discussions with the aim of improving outcomes for the persons living with dementia and their caregivers. We recommend considering the development of dementia friendly organizations/communities for people living with dementia.111-114 2C (91%) |
| 5. Case management is defined as the introduction, modification, or removal of strategies to improve the coordination and continuity of delivery of services which includes the social aspects of care. We recommend considering the use of case management for people living with dementia.115-118 2B 93% |
3.4 | Use of neuroimaging and fluid biomarkers

The imaging biomarkers groups extended the previous consensus work by incorporating new research published since 2012 especially systematic reviews and meta-analyses and guidelines and task force documents. We have refined our suggestions on the following topics: (1) indications for structural imaging; (2) suggestions for computed tomography (CT) sections and magnetic resonance imaging (MRI) sequences; (3) use of semi-quantitative scales and quantification software; (4) the role of fluorodeoxyglucose (FDG) PET and single-photon emission computed tomography (SPECT) in differential diagnosis; (5) specific updates on amyloid imaging and cerebrospinal fluid (CSF) amyloid assays in the Canadian context; and (6) the potential role of SPECT DaT scans in Lewy Body dementia (Table 4).

3.5 | Non-cognitive markers of dementia

Although cognitive impairment is the hallmark of AD and related dementias, non-cognitive markers may be early non-invasive biomarkers. We have divided our search into five main non-cognitive domains that associate with incident dementia: motor function, sensory function (hearing, vision, and olfaction), neurobehavioral symptoms, frailty, and sleep markers. Recommendations were targeted to both primary care clinics and to specialized memory clinics, answering the two main research and clinical questions: (1) What are the non-cognitive and functional changes associated with developing dementia?; and (2) What are the potential sensory, motor, behavioral, sleep, or frailty markers that have been shown to serve as potential predictors of dementia? (Table 5).

3.6 | Risk reduction

As dementia prevention and fluid increasingly seems plausible, CCCDDTD has addressed risk reduction in this iteration. We took the approach that most dementia occurs in late life and typically has multiple causes building on updates from a 2017 comprehensive overview of dementia prevention. We supplemented information (when present) with updates, especially focusing on Canadian data.
offer recommendations on interventions that appear to have importance both across the life course and in primary, secondary, and sometimes tertiary prevention including: (1) nutrition, (2) physical exercise, (3) hearing loss, (4) sleep, (5) cognitive training and rehabilitation, (6) social engagement and education, (7) frailty, (8) and medications (Table 6).

### 3.7 | Psychosocial and non-pharmacological interventions

The psychosocial and non-pharmacological interventions encompass a broad range of interventions and typically aim at improving cognition, symptoms, or well-being (including that of caregivers), or at adapting organizations and communities to the needs of people living with dementia and their caregivers. For the first time, the CCCDTD created a working group on these interventions. We synthesized published meta-analysis and reviews and provide five recommendations of both individual level and community level interventions, as both have the potential to improve outcomes for people living with dementia (Table 7).

### 3.8 | Deprescription of medications used to treat dementia

Acknowledging that many individuals who are affected by dementia can have symptomatic benefits with treatment, there are also situations in which cognitive enhancers (cholinesterase inhibitors and memantine) may not be beneficial or when the balance of benefits to potential harm may change. Evidence-based recommendations are provided for situations in which cognitive enhancers should be discontinued, taking into account the specific goals of the person with dementia and their caregivers, the underlying indication for the cognitive enhancer and type of dementia, and the potential risks and benefits of continuing treatment (Table 8).

### 4 | CONCLUSIONS

We hope that these evidence-based recommendations will be useful to clinicians and policy makers as well as the public at large. We do appreciate that 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.

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