5th CANADIAN CONSENSUS CONFERENCE ON THE DIAGNOSIS & TREATMENT OF DEMENTIA: IMPACT ON CLINICAL PRACTICE

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Co-chairs

POTENTIAL CONFLICTS SG

- Scientific advisor to Boehringer, Schwabe, TauRx
- Research funding from CIHR, NIH, Weston Brain Institute
- DSMB member for ADCS, ATRI, Banner Health

POTENTIAL CONFLICTS - ZI

- Scientific advisor/consultant to Janssen, Lundbeck, Otsuka, Sunovion
- Research funding from CIHR, Brain Canada, CABHI, NIA, Janssen

SPECIAL THANKS

- Nathalie Bélanger and Victor Whitehead from CCNA for helping with voting
- Christine Turenko for helping with logistics
- The *Réseau québecois de recherche sur le vieillissement, the Réseau des cliniques mémoire du Québec* and the CCNA-KT for funding

AGENDA

- History of the CCCDTD
- Process for reaching consensus
- What is new this time?
- Highlights of conclusions
- Potential clinical impacts

OVERALL AIMS OF THE CCCDTD

- Formulate recommendations for use by all interested clinicians
- Based on published data and experience when the literature is incomplete or equivocal.
- Participation of multiple disciplines

HISTORY OF CCCDTD - 1

- 1989 Attention to ‘reversible dementias’; define the minimal workup including CT, criteria on when to refer to a specialist
- 1998 Definitions of the various causes of dementia, including ‘mixed’ types
- 2001 Update of 1998 adding MCI

HISTORY OF CCCDTD - 2

- 2006 Updates on clinical definition of AD (DSM-IV, NINCDS); opinions on neuropsychological testing, on use of CSF
- 2012 Updates on clinical definition of AD starting in ‘prodromal stage’ (IWG/NIA-AA); definition of VCI

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PROCESS TO REACH CONSENSUS - 1

- Steering committee selects topics of clinical relevance to Canadians
- Workgroups study specific topics
- Recommendations are formulated based on literature review, using GRADE system (level 1 and 2 only)
- Voting on line for all workgroup members

PROCESS TO REACH CONSENSUS - 2

- Recommendations scoring between 60% and 79% are discussed in a face-to-face meeting with a 2nd vote for revised recommendations
- Steering committee writes an overview of conclusions
- Each workgroup publishes its literature review with detailed discussion

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TOPICS OF CCCDTD5 - 1

- *Diagnostic criteria for AD*

  Gauthier & Chertkow
- *Diagnostic criteria for VCI*

  Smith & Black
- *Use of brain imaging and liquid* biomarkers

  Soucy & Rosa-Neto
- *Deprescription of anti-dementia drugs*

  Herrmann & Seitz

TOPICS OF CCCDTD5 - 2

- *Psychosocial interventions*

  Sivanantha & Vedel
- *Early cognitive detection of AD*

  Ismail & Laforce Jr.
- *Early non-cognitive detection*

  Montero-Odasso & Camicioli
- *Risk reduction*

  Rockwood & Smith

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HIGHLIGHTS OF CONCLUSIONS
Research diagnostic criteria for AD

- 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. (94%)
- 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. (87%)
- 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. (100%)

HIGHLIGHTS OF CONCLUSIONS
Vascular Cognitive Impairment - 1

- MRI is recommended over CT for investigating vascular cognitive impairment. (96%)
- Use of standardized criteria (one of: the Vascular Behavioral and Cognitive Disorders (VAS-COG) Society criteria, Diagnostic and Statistical Manual of Mental Disorders (DSM)-V, 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. (100%)
- Because treatment of hypertension may reduce risk of dementia, clinicians should assess, diagnose, and treat hypertension according to guidelines from Hypertension Canada. (98%)

HIGHLIGHTS OF CONCLUSIONS
Vascular Cognitive Impairment - 2

- 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. (96%)
- 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 (83%)
- 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 individual patients. (85%)

HIGHLIGHTS OF CONCLUSIONS
Use of brain imaging

- Neuroimaging is recommended in most situations (76%; 100%)
- MRI is recommended over CT, especially given its higher sensitivity to vascular lesions as well as for some subtypes of dementia and rarer conditions. (87%)
- 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. (82%). 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.

HIGHLIGHTS OF CONCLUSIONS
Fluid Biomarkers

- 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 AD pathophysiology (1C) (78%; 100%)
- CSF analysis can also be considered in dementia patients with diagnostic uncertainty and predominance of language, visuospatial, dysexecutive, or behavioural features to r/o AD pathophysiology (1C) (78%; 100%)

HIGHLIGHTS OF CONCLUSIONS
Deprescription of anti-dementia drugs - 1

- For individuals taking a ChEI for AD, PDD, LBD or VaD for >12 months, discontinuation should be considered if: a)There has been a clinically meaningful worsening of dementia as reflected in changes in cognition, functioning or global assessment over the past 6 months in the absence of other medical conditions (e.g. presence of delirium, significant concomitant medical illness) or environmental factors (e.g. recent transition in residence) that may have contributed significantly to the observed decline. b) No clinically meaningful benefit was observed at any time during treatment (improvement, stabilization, decreased rate of decline) c) The individual has severe or end-stage dementia (dependence in most basic activities of daily living, inability to respond to environment or limited life expectancy) d) Development of intolerable side-effects (e.g. severe nausea, vomiting, weight loss, anorexia, falls) e) Medication adherence is poor and precludes safe ongoing use of the medication or inability to assess the effectiveness of the medication. (98%)

HIGHLIGHTS OF CONCLUSIONS
Deprescription of anti-dementia drugs - 2

- Cholinesterase inhibitors should not be discontinued in individuals who currently have clinically meaningful psychotic symptoms or agitation and aggression until these symptoms have stabilized unless these symptoms appear to have been worsened by the initiation of a CHEI or an increase in CHEI dose (2B). (79%; 100%)
- Individuals who have had a clinically meaningful reduction in neuropsychiatric symptoms(e.g. psychosis) with cognitive enhancers should continue to be treated with the cognitive enhancer even if there is evidence of cognitive and functional decline. (91%)
- Cholinesterase inhibitors and memantine should be deprescribed for individuals with mild cognitive impairment. (89%)

HIGHLIGHTS OF CONCLUSIONS
Psychosocial interventions

- We recommend exercise for people living with dementia. (93%)
- We recommend considering group cognitive stimulation therapy for people living with mild to moderate dementia. (93%)
- We recommend considering psychosocial and psychoeducational interventions for caregivers on people living with dementia. (96%)
- We recommend considering the development of dementia friendly organizations/communities for people living with dementia. (91%)
- We recommend considering the use of case management for people living with dementia. (93%)

HIGHLIGHTS OF CONCLUSIONS
Early detection of AD-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 (95%)
- 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. 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 (95%)

HIGHLIGHTS OF CONCLUSIONS
Early detection of AD-2

- 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). Grade 1B

- Obtaining corroborative history is essential, and has prognostic significance. Reliable informant information should be obtained for changes in cognition, function, and behaviour/neuropsychiatric symptoms (i.e. new onset symptoms vs. chronic or longstanding symptoms). Grade 1B

HIGHLIGHTS OF CONCLUSIONS
Early non-cognitive detection - 1

- 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. (91%)
- We recommend that frailty is assessed as a marker of future dementia in primary care and memory clinics. (87%)
- 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. (96%)
- Corroborative information from a reliable informant is recommended. Using a validated informant-rated scale like the NPI-Q or MBI-C will operationalize assessment of NPS, especially in primary care.(91%)

HIGHLIGHTS OF CONCLUSIONS
Early non-cognitive detection - 2

- A careful sleep history, including assessment of sleep time, insomnia, daytime sleepiness, napping, and REM sleep behaviour 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. (91%)
- There is enough observational evidence that hearing impairment is associated with the development of dementia. We recommend to asses and record hearing impairment in primary clinics as a dementia risk factor. (87%)

HIGHLIGHTS OF CONCLUSIONS
Risk reduction - 1

- That exposure to medications known to exhibit highly anticholinergic properties be minimized in older persons. Alternative medications should be used for specific indications where medications with anticholinergic properties are indicated. (e.g. depression, neuropathic pain, urge type urinary incontinence) (98%)
- 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. (83%)
- 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. (96%)
- We recommend adherence to a Mediterranean diet to decrease the risk of cognitive decline. (90%)

HIGHLIGHTS OF CONCLUSIONS
Risk reduction - 2

- We recommend physical activity interventions to reduce the risk of dementia, including AD and vascular dementia. (94%)
- We recommend that interventions to manage frailty be used to reduce the overall burden of dementia in older adults. (81%)
- 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. (96%)
- Adults with sleep apnea should be treated with CPAP, which may improve cognition and decrease the risk of dementia. (96%)
- Avoiding severe (<5h) sleep deprivation, and targeting 7-8 hours of sleep per night, may improve cognition and decrease the risk of dementia. (94%)

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POTENTIAL CLINICAL IMPACTS - 1

- Screening for cognitive impairment should be done in primary care setting when there are symptoms or suspicion based on other clinical factors, including frailty, parkinsonism, first episode psychiatric symptoms in later life.

POTENTIAL CLINICAL IMPACTS - 2

- Brain MRIs should be requested if there is suspicion of a vascular etiology or component to a cognitive decline
- [18F]-FDG PET is recommended in case of diagnostic uncertainty after a consultation by a cognitive disorder specialist
- A SPECT rCBF is a second choice

POTENTIAL CLINICAL IMPACTS - 3

- Arterial hypertension should be treated based on guidelines from Hypertension Canada
- The benefit of ASA is unclear in the absence of a history of stroke
- The use of drugs with anticholinergic actions should be minimized in older persons

POTENTIAL CLINICAL IMPACTS - 4

- Cholinesterase inhibitors should be continued if the clinical indication is appropriate (AD, PDD, DLB, VaD), if the patient had a reduction in neuropsychiatric symptoms

POTENTIAL CLINICAL IMPACTS - 5

- Patient should be offered exercise, groups cognitive stimulation, case management
- Caregivers should received psychosocial and psychoeducational interventions

POTENTIAL CLINICAL IMPACTS - 6

- A variety of cognitively stimulating activities, adherence to a Mediterranean-style diet, physical activities of moderate intensity may improve cognitive outcomes among older adults
- Sleep apnea should be looked for and treated

Next Steps

- Publication plan
- Primary and group papers
- KT through CCNA and other organizations