



**Third** Canadian Consensus Conference on **D**iagnosis and **T**reatment of **D**ementia

# **3<sup>rd</sup> Canadian Consensus Conference on Diagnosis and Treatment of Dementia**

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**146 APPROVED RECOMMENDATIONS  
FINAL- JULY , 2007**

## **Topic 1: Assessment and management of risk factors, and primary prevention strategies**

1. There is good evidence to treat systolic hypertension (>160mm) in older individuals. In addition to reducing the risk of stroke, the incidence of dementia may be reduced. The target BP should be 140mm or less. (Grade A, Level 1)
2. While ASA and statin medications following myocardial infarction; antithrombotic treatment for non-valvular atrial fibrillation; and correction of carotid artery stenosis >60% have been shown to reduce the risk of stroke, there is insufficient evidence to recommend for or against these measures for the specific purpose of primary prevention of dementia. (Grade C, Level 1)
3. While there are many reasons for treating type 2 diabetes, hyperlipidemia and hyperhomocysteinemia, there is insufficient evidence to recommend treatment of these conditions for the specific purpose of reducing the risk of dementia. (Grade C, Level 2)
4. There is insufficient evidence to recommend for or against the prescription of NSAIDs for the sole purpose of reducing the risk of dementia. (Grade C, Level 2)
5. There is good evidence to avoid the use of estrogens alone or together with progestins for the sole purpose of reducing the risk of dementia. (Grade E, Level 1)
6. While there is insufficient evidence to make a firm recommendation, physicians may advocate for strategies including legislation, to reduce the risk of serious head injuries. (Grade C, Level 2)
7. While there is insufficient evidence to make a firm recommendation, physicians may advise their patients about, and advocate for, appropriate protective clothing during administration of pesticides, fumigants, fertilizers and defoliants. (Grade C, Level 2)
8. There is insufficient evidence to recommend for or against supplementation with vitamins E or C for the prevention of dementia. (Grade C, Level 2) High dose vitamin E ( $\geq 400$  units/day) is associated with excess mortality and should not be recommended. (Grade E, Level 1)
9. While recommendations may be made on other grounds (such as part of a healthy lifestyle), there is insufficient evidence to recommend for, or against higher levels of physical or mental activity for the specific purpose of reducing the incidence of dementia. (Grade C, Level 2)
10. While there is insufficient evidence to make a firm recommendation for the primary prevention of dementia, physicians may advocate for appropriate levels of education and strategies to retain students in appropriate learning environments. (Grade C, Level 2)
11. While there is insufficient evidence to make a firm recommendation for the primary prevention of dementia, physicians may choose to advise their patients about the potential advantages of increased consumption of fish,

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(Grades/Levels of evidence appear in brackets)

reduced consumption of dietary fat and moderate consumption of wine.  
(Grade C, Level 2)

## **Topic 2: Concept, utility, and management of MCI and CIND**

1. Physicians should be aware that most dementias may be preceded by a recognizable phase of mild cognitive decline. Physicians should be familiar with the concept of mild cognitive impairment (MCI) [or cognitive impairment not dementia (CIND)] as a high risk state for decline and dementia. (Grade B, Level 3)
2. There is currently inadequate evidence to recommend one term or label (MCI, CIND) over another. (Grade B, Level 3)
3. There is inadequate evidence to advise MCI patients and their families that the patient is already showing signs of dementia, or to treat MCI as equivalent to dementia. (Grade C, Level 2)
4. There is fair evidence that physicians should closely monitor individuals who have MCI or CIND, because of the known increased risk of both dementia and death that has been documented. (Grade B, Level 2)
5. 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 (24-30), tests such as the MoCA, DemTect, or CMC could be administered. These would help to demonstrate objective cognitive loss. (Grade B, Level 2)
6. There is good evidence that the addition of in-depth neuropsychological testing can be recommended to aid in the confirmation of the diagnosis. (Grade A, Level 1)
7. The evidence at the present time is insufficient to conclude that organized cognitive intervention is beneficial to preventing progression in MCI or warrants prescription. (Grade C, Level 1)
8. There is fair evidence that physicians and therapists should promote engagement in cognitive activity as part of an overall "healthy lifestyle" formulation for elderly individuals with and without memory loss. (Grade B, Level 1)
9. There is fair evidence that physicians and therapists should promote physical activity at an intensity level that is adapted to the persons' overall physical capacities, as part of a "healthy lifestyle" for older individuals with and without memory loss. (Grade B, Level 2)
10. Current evidence is insufficient to conclude that a specific program of physical training warrants prescription in MCI patients in order to prevent progression to dementia. (Grade C, Level 3)
11. There is currently insufficient evidence to recommend for the use of cholinesterase inhibitors in MCI. (Grade C, Level 1)
12. There is currently fair evidence to recommend against the use of NSAIDs in MCI. (Grade D, Level 1)
13. There is currently fair evidence to recommend against the use of estrogen replacement therapy in MCI. (Grade D, Level 1)

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14. There is currently fair evidence to recommend against the use of Ginkgo biloba in MCI. (Grade D, Level 1)
15. There is currently fair evidence to recommend against the use of vitamin E in MCI. (Grade D, Level 1)
16. As vascular risk factors and comorbidities impact on the development and expression of dementia, they should be screened for and treated optimally in MCI. (Grade B, Level 2)

### **Topic 3: Diagnosis and differential diagnosis of dementia for the primary care practitioner and consultant: clinical laboratory, imaging, markers.**

#### **Clinical Aspects of Diagnosis**

1. The diagnosis of dementia remains clinical. There is good evidence to retain the diagnostic criteria currently in use. (Grade A, Level 2)
2. The sensitivity of clinical diagnosis for possible or probable Alzheimer's disease based on the NINDS-ADRDA criteria remains high. The specificity is lower. The continued use of the NINDS-ADRDA criteria is recommended. (Grade A, Level 1)
3. 'Mild' Alzheimer's disease can be diagnosed with a high degree of specificity, when the presenting clinical picture is one of memory impairment. (Grade B, Level 1)
4. The currently available vascular dementia diagnostic criteria have variable accuracy. An integrative approach to vascular dementia diagnosis based on all the available evidence (history, vascular risk factors, physical exam, clinical course, neuroimaging, cognitive impairment pattern) is recommended. (Grade B, Level 2)
5. The clinical features of Dementia with Lewy bodies (DLB) and Parkinson disease dementia (PDD) overlap considerably. At present DLB should be diagnosed when this pattern of dementia occurs before or concurrently with parkinsonism. PDD can be diagnosed when dementia occurs in the context of well-established PD, generally after many years. (Grade B, Level 3)
6. There is frequent co-existence of Alzheimer's disease and Lewy Body neuropathology in subjects presenting with the initial clinical picture of either pathology. At present, it is impossible to propose clinical guidelines that would permit separation of the two diagnoses, and of AD+DLB with a high specificity. (Grade A, Level 2)
7. In patients presenting primarily with progressive decline in language or praxis, or with prominent changes in behavior or personality, Pick Complex Disease also known as fronto-temporal dementia or frontotemporal lobar degeneration should be considered. These disorders of Pick Complex include semantic dementia, frontotemporal dementia behavioral variant (FTD-bv), primary progressive aphasia, corticobasal degeneration, progressive supranuclear palsy and FTD with motor neuron disease (FTD-MND). These disorders have clinical features that are distinctive and are best referred for specialist care (Grade A, Level 2)
8. When gait apraxia, or urinary incontinence occur early in the course of dementia, Normal Pressure Hydrocephalus should be considered and should be supported by CT or MRI. Specialist referral is advised for further assessment. The diagnostic workup may include the removal of a large CSF volume with documentation of clinical response, if surgical intervention is considered an appropriate option. (Grade B, Level 2)

9. Rapidly progressing dementia associated with myoclonus and an EEG with the presence of periodic sharp waves is typical of Creutzfeldt-Jakob Disease (CJD). There are three clinical criteria sets in use to diagnose CJD, all with some specificity. The recognition of rapid progression in a dementia syndrome, should by itself suggest the possibility of CJD. (Grade A, Level 2)
10. CJD is a distinctively rapidly progressive dementia that in Canada requires reporting to the CJD Surveillance Network and requires special infection control procedures. Its diagnosis is supported by a positive 14-3-3 test on CSF, by an abnormal MRI scan, with either basal ganglia high signal on T2 or abnormalities on diffusion weighted imaging, and by a progressively worsening EEG with periodic complexes. Specialist referral is recommended. (Grade B, Level 2)

## **Neuropsychological Evaluations**

### **Recommendations for Brief Cognitive Tests**

1. The MoCA and the DemTect are more sensitive to MCI than the MMSE. Their use is recommended when mild cognitive impairment is suspected. There is insufficient evidence to recommend one test over the other. (Grade B, Level 2 - because replication in different settings, particularly the general practice setting, is required)
2. There is insufficient evidence to recommend the Delayed 3-trial MMSE adaptation, the STMS, and the SSST for the detection of MCI. (Grade C, Level 2)
3. A range of brief cognitive tests, including the MoCA, DemTect, BNA, GPCOG, and the 7MS may be more accurate than the MMSE in discriminating dementia from the normal state. There is insufficient evidence to recommend one test over the others. (Grade B, Level 2 - because replication studies are needed) .
4. The distinction between MCI and AD is important and is currently made on the basis of clinical assessment of cognition and function. (Grade A, Level 3).
5. Brief cognitive tests may aid in the assessment of this distinction between MCI and AD. The DemTect and the STMS can be recommended as they have established cut-points for both MCI and AD. (Grade B, Level 2)

### **Recommendations for Neuropsychological Assessment**

6. The diagnosis and differential diagnosis of dementia is currently a clinically integrative one. Neuropsychological assessment alone cannot be used for this purpose and should be used selectively in clinical settings. (Grade B, Level 2)
7. Neuropsychological assessment may aid in:
  - a) Addressing the distinction between normal aging, MCI-CIND and early dementia; (Grade B, Level 2)

- b) Addressing the risk of progression from MCI-CIND to dementia or AD; (Grade B, Level 2)
- c) Differential diagnosis of dementia and other syndromes of cognitive impairment; (Grade B, Level 2)
- d) Determining whether there has been progression of cognitive impairment or the development of new impairment(s) to assist in management. (Grade A, Level 3)

## **Biomarkers**

### **To Primary Care Physicians**

1. Biological markers for the diagnosis of AD should not, at this juncture, be included in the battery of tests routinely used by primary care physicians to evaluate subjects with memory loss. (Grade C, Level 3) Consideration for such specialized testing in an individual case should prompt referral of the patient to a neurologist, psychiatrist, or geriatrician engaged in dementia evaluations or a Memory Clinic.

### **To Specialists**

2. Although highly desirable, there currently exist no blood- or urine-based AD diagnostics that can be unequivocally endorsed for the routine evaluation of memory loss in the elderly. (Grade C, Level 3) The non-invasiveness of such tests, if and when they become available, would be suitable for mass screening of subjects with memory loss presenting to specialists in their private offices and Memory Clinics.
3. Due to their relative invasiveness and availability of other fairly accurate diagnostic modalities (clinical, neuropsychological, and neuroimaging), CSF biomarkers should not be routinely performed in all subjects undergoing evaluation for memory loss. (Grade D, Level 2)
4. CSF biomarkers may be considered in the differential diagnosis of AD where there are atypical features and diagnostic uncertainty. (Grade B, Level 2) For example, CSF biomarkers may prove useful in differentiating frontal variants of AD from FTD.
5. When a decision to obtain CSF biomarkers is made, combined A $\beta$ <sub>1-42</sub> and p-tau concentrations should be measured by validated ELISA. (Grade A, Level 1) It may be best to convey the CSF samples to a centralized facility (commercial or academic) with a track record in generating high-quality, reproducible data.
6. CSF biomarker data in isolation are insufficient to diagnose or exclude AD. (Grade C, Level 3) They should be interpreted in light of clinical, neuropsychological, other laboratory and neuroimaging data available for the individual under investigation.

## **Structural Neuroimaging**

1. There is fair evidence to support the selective use of CT or MRI scanning in the work-up for dementia – per 1999 Guidelines. (Grade B, Level 2)
2. There is fair evidence to support use of structural neuroimaging to rule in concomitant cerebrovascular disease that can affect patient management. (Grade B, Level 2)
3. There is fair evidence to support the use of structural neuroimaging to track the progression of AD in clinical trials, especially if the morphometry is combined with neuropsychological testing. (Grade B, Level 2)

## **Functional Neuroimaging**

1. There is fair evidence that functional imaging with PET or SPECT scanning might assist specialists in the differential diagnosis of dementia, particularly those with questionable early stage dementia or those with frontotemporal dementia. There is variability across centers, with requisite expertise in these modalities that needs to be taken into account in determining utility. (Grade B, Level 2)
2. fMRI and MRS scanning are not recommended for use by family physicians or specialists to make or differentiate a diagnosis of dementia in people presenting with cognitive impairment. They remain very promising research tools. (Grade D, Level 3)

## **Lab Tests**

1. It is recommended that serum Cbl levels be determined in all older adults suspected of dementia or cognitive decline. (Grade B, Level 2)
2. Older adults found to have low Cbl levels should be treated with Cbl (either oral or parenteral forms), because of potential improvement of cognitive function and the deleterious effects of low Cbl levels on multiple organ systems, besides the effects on cognition. (Grade B, Level 2)
3. There is currently insufficient evidence to support the need for serum homocysteine (tHcy) levels to be determined in older adults suspected of dementia or cognitive decline (Grade C, Level 3)
4. There is currently insufficient evidence that treatment of elevated serum homocysteine (tHcy) levels affects cognition. (Grade C, Level 3)
5. Determination of serum folic acid or RBC folate in older adults in Canada is optional, and may be reserved for patients with celiac disease, inadequate diets, or other conditions that prevent them from ingesting grain products. (Grade E, Level 2)

## **Topic 4: Genetics and Dementia: Risk Factors, Diagnosis, & Management**

### **Predictive genetic testing for asymptomatic “at risk” individuals with an apparent autosomal dominant inheritance, and a family-specific mutation has been identified**

1. With appropriate pre-and post-testing counselling, predictive genetic testing (PGT) can be offered to “at risk” individuals (Grade B, Level 2). Examples:
  - a) First-degree relatives of an affected individual with the mutation (e.g., children and siblings);
  - b) First cousins of an affected individual if the common ancestors (parents who were siblings) died before the average age of onset of dementia in the family;
  - c) Nieces and nephews of affected individuals whose parent (sibling of the affected individual) died well before the average age of onset of dementia in the family;
  - d) PGT in minors is not generally offered in Canada, but occasionally may be considered on a case-by-case basis by the relevant medical ethics committee(s);
  - e) Individuals who are not “at risk” for the inherited disease do not require testing.
2. In young persons (60 years or younger) presenting with an early onset dementia, it is sometimes worthwhile to test for the most common mutations based on the “best estimate” diagnosis (e.g., in early onset AD, one might test for the most common mutations in PS1, APP). (Grade B, Level 2) If a mutation is identified, it would have direct implications for offspring of the individual (if a de novo mutation is assumed). Conversely, it would also be important to test other family members such as parents and siblings for possible non-penetrance of a mutation.
3. Careful review of all available documentation (examination, clinical records, autopsy reports, etc.) on reportedly affected relatives is essential to rule out the heterogeneous causes of dementia in the elderly, including depression, alcoholism, vascular dementia, etc. If appropriate after review, genetic counselling should include the risks associated with an autosomal dominant mode of inheritance as the uppermost risk. It is advisable, for the benefit of future generations, to bank DNA and/or autopsy material from affected individuals in such families in case novel gene mutations may be discovered in the future. (Grade B, Level 2)

### **Prenatal Genetic Testing**

4. Prenatal testing for a known family mutation associated with adult onset dementia is technically possible. However, this is not generally offered in Canada. The ethical implications are complex and need to be explored

further. (Grade C, Level 3). Requests may be considered on a case-by-case basis by the relevant medical ethics committee(s).

### **Ethical issues in Genetic Testing**

5. After careful genetic counselling with family members, if it is decided that genetic testing and/or banking of DNA (or autopsy material) for future studies is in the best interest of family members, this may be done even without the consent or assent of the affected individual who is not cognitively competent, if consent from the family is given. (Grade B, Level 2) However, extreme care must be taken to minimize any distress the patient may experience while the sample is being obtained. In cases where family members, after extensive counselling, cannot agree on a plan, the case may have to go before a medical ethics committee.
6. Concerned family members should have appropriate pre- and post-test counselling available to be able to make informed decisions. (Grade B, Level 2) In cases of conflict among family members, medical ethics committees may become involved.

### **Genetic susceptibility risk factors**

7. Genetic screening with APOE genotype in asymptomatic individuals in the general population is not recommended because of the low specificity and sensitivity. (Grade E, Level 2)
8. Genetic testing with APOE genotype is not recommended for the purpose of diagnosing AD because the positive and negative predictive values are low. (Grade E, Level 2)

## \Topic 5: Management of mild to moderate Alzheimer's disease

1. Most patients with dementia can be assessed and managed adequately by their primary care physicians. However, in order to assist them in meeting the needs of patients and their caregivers, it is recommended that:
  - a) All patients with dementia and their families who consent be referred to the local chapter of the Alzheimer Society (e.g., *First Link* program where available); and,
  - b) Primary care physicians should be aware of the resources available for the care of those with dementia in their community (e.g., support groups, adult day programs) and to make appropriate referrals to them. (Grade B, Level 3)
2. The referral/consultation process is essential to the delivery of high quality health care. In the care of a patient with mild to moderate dementia, reasons to consider referral to a geriatrician, geriatric psychiatrist, neurologist, or other health care professional (e.g., neuropsychologist, nurse, nurse practitioner, occupational therapist, physical therapist, psychologist, social worker, other) with the appropriate knowledge and expertise in dementia care would include:
  - a) Continuing uncertainty about the diagnosis after initial assessment and follow-up;
  - b) Request by the patient or the family for another opinion;
  - c) Presence of significant depression, especially if there is no response to treatment;
  - d) Treatment problems or failure with specific medications for AD;
  - e) Need for additional help in patient management (e.g., behavioural problems, functional impairments) or caregiver support;
  - f) Genetic counseling when indicated; and,
  - g) If the patient and/or family express interest in either diagnostic or therapeutic research studies that are being carried out by the recipient of the consult request. (Grade B, Level 3)
3. The care and management of patients with dementia from specific cultural groups should take into account the risk of isolation, the importance of culturally appropriate services, and issues that arise in providing caregiver support. (Grade B, Level 3)
4. Recommendations with regards to the general medical care of a patient with a mild to moderate dementia –
  - a) Patients with mild to moderate dementia, when hospitalized, should be identified as being at increased risk for delirium. They should be offered multicomponent interventions including orienting communication, therapeutic activities, sleep enhancement strategies, exercise and mobilization, provision of vision and hearing aids, and/or

- oral repletion of dehydration to decrease their risk of developing delirium. (Grade B, Level 2)
  - b) Comorbidities of patients with mild to moderate AD should be appropriately managed. (Grade B, Level 3)
  - c) The management of other chronic medical conditions may have to be modified in the setting of a dementia. In general there should be less reliance on patient self-care and a concomitant increase in the role played by care-givers. (Grade B, Level 3)
5. Recommendations about the use of medications in the setting of a mild to moderate dementia –
- a) Determination of how medications are being consumed and identification of any problems/concerns with medication management, including poor adherence, should be done on all patients with mild to moderate dementia. If problems are detected, in particular with adherence, the use of compliance aids or the assumption of medication management by another party will be necessary. The effectiveness of any alterations in medication management will have to be assessed. (Grade B, Level 3)
  - b) Even when the patient is safely self-managing their medications, there should be planning for the involvement of a third party in the management of medications for all patients with a progressive dementia, as this will eventually become necessary in nearly all patients. (Grade B, Level 3)
  - c) The use of medications with anticholinergic effects should be minimized in persons with AD. (Grade D, Level 3)
6. Ethico-legal recommendations –
- a) Although each case should be considered individually, in general the diagnosis of dementia should be disclosed to the patient and family. This process should include a discussion of prognosis, diagnostic uncertainty, advance planning, driving issues, treatment options, support groups, and future plans. (Grade B, Level 3)
  - b) Primary care physicians should be aware of the pertinent laws in their jurisdiction about informed consent, the assessment of capacity, the identification of a surrogate decision-maker, and the responsibilities of physicians in these matters. (Grade B, Level 3)
  - c) While patients with AD retain capacity, they should be encouraged to update their will and to enact both an advance directive and an enduring power of attorney. (Grade B, Level 3)
7. Recommendations for non-pharmacological interventions for the management of the cognitive and functional limitations arising from mild to moderate AD –
- a) There is insufficient research evidence to come to any firm conclusions about the effectiveness of cognitive training/cognitive rehabilitation in improving and/or maintaining cognitive and/or functional performance in persons with mild to moderate dementia. (Grade C, Level 1)

- b) Further research is required to be able to conclude that cognitive training/cognitive rehabilitation is effective in improving cognitive and/or functional performance in persons with mild to moderate dementia. (Grade B, Level 2)
  - c) Although there is some indication of a beneficial impact on IADL and ADL, there is insufficient evidence to make firm conclusions about the effectiveness of environmental interventions in promoting functional performance in persons with mild to moderate dementia. (Grade C, Level 1)
  - d) There is good evidence to indicate that individualized exercise programs have an impact on functional performance in persons with mild to moderate dementia. (Grade A, Level 1)
  - e) For other non-pharmacological therapeutic interventions, there is insufficient evidence to allow any conclusions being made about their efficacy in improving or maintaining functional performance in persons with mild to moderate dementia. (Grade C, Level 1)
8. Primary care physicians should be able to administer and interpret brief measures of functional activities and cognitive abilities, or refer to health care professionals with the required knowledge and expertise. (Grade B, Level 3)
  9. After treatment has been started, patients should be reassessed regularly by the appropriate health care professional involved in their care. (Grade B, Level 3)
  10. Records should be kept such that stabilization, improvement, or persisting deterioration in treated patients will be determinable. (Grade B, Level 3)
  11. In monitoring the response to therapy of patients with dementia, the input of caregivers (where available) should be sought. They can provide information on the patient's cognition, behavior, and social and daily functioning. (Grade B, Level 3)
  12. If the attending primary care physician is unable to perform the assessments required to gauge response to therapy, referral to another health care professional with knowledge and expertise in dementia care (e.g., other physician, nurse, occupational therapist) or a service (e.g., memory clinic) willing to perform such assessments is advised. (Grade B, Level 3)
  13. Primary care physicians should be able to communicate appropriate information concerning dementia, including realistic treatment expectations to their patients and their families. (Grade B, Level 3)
  14. Recommendations regarding the use of cholinesterase inhibitors –
    - a) All three cholinesterase inhibitors available in Canada are modestly efficacious for mild to moderate AD. They are all viable treatment option for most patients with mild to moderate AD. (Grade A, Level 1)
    - b) While all three cholinesterase inhibitors available in Canada have efficacy for mild to moderate AD, equivalency has not been established in direct comparisons. Selection of which agent to be used will be based on adverse effect profile, ease of use, familiarity, and beliefs

- about the importance of the differences between the agents in their pharmacokinetics and other mechanisms of action. (Grade B, Level 1)
- c) All physicians prescribing these agents should be aware of the contraindications and precautions with the use of cholinesterase inhibitors. (Grade B, Level 3)
  - d) If adverse effects occur with a cholinesterase inhibitor, the agent should either be discontinued (if the side effects are judged to be disabling and/or dangerous), or the dose of the agent should be decreased with an option to retry the higher dose after two to four weeks if the lower dose is tolerated (if the side effects are judged to be minor in severity). (Grade B, Level 3)
  - e) If nausea and/or vomiting occur with the use of a cholinesterase inhibitor, review how the medication is being taken (e.g., dose, frequency, with or without food, evidence of an unintentional overdose) and consider: modifying the prescription (e.g. lower dose); the responsibility for administration (e.g., caregiver taking over from the patient); the directions given to the patient (e.g., with food); or, stopping the agent. While anti-emetics can be used for nausea and/or vomiting, a number of them (e.g., dimenhydrinate, prochlorperazine) have anticholinergic properties that can lead to adverse cognitive effects. (Grade B, Level 3)
  - f) Clinicians should consider the possible contributing role of cholinesterase inhibitors in new-onset or worsening medical presentations, and the potential risk of co-prescribing cholinesterase inhibitors and other drugs to patients with dementia. (Grade B, Level 2)
  - g) Patients can be switched from one cholinesterase inhibitor to another. A decision to make a switch is based on the judgment of the prescribing physician and the patient (or their proxy) about the relative benefits and risks of making a change in the patient's pharmacotherapy. (Grade B, Level 3)
  - h) Patients can be switched from a cholinesterase inhibitor to memantine (note: please see recommendation 15b). The decision of when to make a switch is based on the judgment of the prescribing physician and the patient (or their proxy). (Grade B, Level 3)
15. Recommendations regarding the use of memantine –
- a) Memantine is an option for patients with moderate to severe stages of AD. (Grade B, Level 1) Its use in mild stages of AD is not recommended. (Grade D, Level 1)
  - b) Combination therapy of a cholinesterase inhibitor and memantine is rational (as the medications have different mechanisms of action), appears to be safe, and may lead to additional benefits for patients with moderate to severe AD. This would be an option for patients with AD of a moderate severity. (Grade B, Level 1)
16. Medications for the treatment of cognitive and functional manifestations of AD should be discontinued when:
- a) The patient and/or their proxy decision maker decides to stop;

- b) The patient refuses to take the medication;
  - c) The patient is sufficiently non-adherent with the medication that continued prescription of it would be useless, and it is not possible to establish a system for the administration of the medication to rectify the problem;
  - d) There is no response to therapy after a reasonable trial;
  - e) The patient experiences intolerable side effects;
  - f) The comorbidities of the patient make continued use of the agent either unacceptably risky or futile (e.g., terminally ill); or,
  - g) The patient's dementia progresses to a stage where there is no significant benefit from continued therapy. (Grade B, Level 3)
17. After stopping therapy for AD, patients should be carefully monitored and if there is evidence of a significant decline in their cognitive status, functional abilities, or the development/worsening of behavioural challenges, consideration should be given to re-instating the therapy. (Grade B, Level 3)
18. Recommendations with regard to supplements, herbal preparations, and other medications for the cognitive and functional manifestations of AD and dementia –
- a) High-dose (i.e., 400+ iu/day) vitamin E supplementation is not recommended for the treatment of AD. (Grade E, Level 1)
  - b) The use of the synthetic antioxidant idebenone is not recommended for the treatment of AD. (Grade E, Level 1)
  - c) The administration of vitamin B1, B6, B12, and/or folic acid supplements to persons suffering from AD who are not deficient in these vitamins is not recommended. (Grade D, Level 3)
  - d) There is insufficient evidence to allow for a recommendation either for or against the use of Ginkgo biloba in the treatment of dementia. Further methodologically sound trials are required. (Grade C, Level 1)
  - e) The use of an anti-inflammatory drug is not recommended for the treatment of the cognitive, functional, or behavioural manifestations of a dementia. (Grade D, Level 1)
  - f) The use of a HMG-CoA reductase enzyme inhibitor is not recommended for the treatment of the cognitive, functional, or behavioural manifestations of a dementia. (Grade D, Level 3)
  - g) Hormone replacement therapy (estrogens combined with a progestagen) or estrogen replacement therapy (estrogen alone) is not recommended for the cognitive impairments of women with AD. (Grade D, Level 1)
  - h) There is insufficient evidence to recommend the use of androgens (e.g., testosterone) to treat AD in men. (Grade C, Level 1)
  - i) There is negative, inconclusive, or conflicting evidence for a number of other agents proposed as potential therapies for the cognitive and behavioural manifestations of AD. Their use cannot be recommended at this time. (Grade C or D, Levels 1-3 – varies between agents)

19. Assessment of patients with mild to moderate AD should include measures of behavior and other neuropsychiatric symptoms. (Grade B, Level 3)
20. The management of BPSD should include a careful documentation of behaviours and identification of target symptoms, a search for potential triggers or precipitants, recording of the consequences of the behaviour, an evaluation to rule out treatable or contributory causes, and consideration of the safety of the patient, their caregiver, and others in their environment. (Grade B, Level 3)
21. Recommendations with regard to the management of depressive symptoms in the setting of mild to moderate dementia –
  - a) As depressive syndromes are frequent in patients with dementia, physicians should consider diagnosing depression when patients present with the subacute development (e.g., weeks, rather than months or years) of symptoms characteristic of depression such as behavioural symptoms, weight and sleep changes, sadness, crying, suicidal statements, or excessive guilt. (Grade B, Level 3)
  - b) Depressive symptoms that are not part of a major affective disorder, severe dysthymia, or severe emotional lability should initially be treated non-pharmacologically. (Grade B, Level 3)
  - c) If the patient had an inadequate response to the non-pharmacological interventions or has a major affective disorder, severe dysthymia, or severe emotional lability, a trial of an antidepressant should be considered. (Grade B, Level 3)
  - d) If an antidepressant is prescribed to a person with AD, the preferred choice would be an agent with minimal anticholinergic activity, such as an SSRI. (Grade B, Level 3)
22. Recommendations with regard to sleep problems in the setting of a mild to moderate dementia –
  - a) Patients with AD experiencing sleep problems should first undergo a careful assessment for medical illnesses (including pain), psychiatric illnesses (especially depression), potentially contributing medications, environmental factors, and/or poor sleep habits (e.g., daytime naps) that may be adversely affecting sleep. Any identified secondary cause should be managed. (Grade B, Level 3)
  - b) The presence of a REM sleep behaviour disorder in the setting of a dementia would be suggestive of DLB and related conditions. Treatment options would include clonazepam. (Grade B, Level 2)
  - c) Non-pharmacological approaches to sleep disturbances can be effective for patients with AD but a combination of these approaches will likely be required. (Grade B, Level 1)
  - d) When considered clinically necessary, pharmacological interventions for insomnia, including short- to intermediate-acting benzodiazepines and related agents, can be used at the lowest effective doses and for the shortest possible time. (Grade B, Level 3)

23. Recommendations with regard to the management of BPSD in the setting of a mild to moderate dementia –
- a) Non-pharmacological treatment of BPSD should be considered first. Non-pharmacological interventions are often used in combination with pharmacotherapy. (Grade C, Level 1)
  - b) Although there is insufficient evidence regarding the effectiveness of the interventions to strongly advocate for their routine use in the management of BPSD, some persons with dementia may benefit from the following: music; Snoezelen (multi-sensory stimulation); bright light therapy; reminiscence therapy; validation therapy; aroma therapy; and, massage and touch therapy. (Grade C, Level 2)
  - c) Pharmacotherapy for BPSD should be initiated only after consideration, and usually a trial where appropriate, of non-pharmacological interventions. (Grade B, Level 3)
  - d) The presence of visual hallucinations in the setting of mild dementia would suggest that the patient has DLB. Patients with DLB are abnormally sensitive to antipsychotics. If pharmacotherapy is required for the visual hallucinations, a cholinesterase inhibitor should be tried first, if possible. If acute symptom control is required or the cholinesterase inhibitor is ineffective, a cautious trial of an atypical antipsychotic (e.g., very low dose quetiapine) can be attempted. (Grade B, Level 2)
  - e) Medications for BPSD should normally be initiated at a low starting dose and then subsequently titrated carefully based on the patient's response and the presence of adverse effects. (Grade B, Level 3)
  - f) There should be periodic attempts to taper and withdraw medications after a period of three months behavioural stability. (Grade B, Level 3)
  - g) Patients who have mild to moderate AD and neuropsychiatric symptoms can be considered for a trial of a cholinesterase inhibitor and/or memantine for these symptoms. (Grade B, Level 3)
  - h) Treatment of BPSD with cholinesterase inhibitors or memantine should persist until clinical benefits can no longer be demonstrated. (Grade B, Level 3)
24. For the following community-based programs for the management of behavioral disturbances, there is limited high-quality evidence regarding effectiveness. The recommendations are based on one to two RCTs for each program:
- a) Adult day care (greater involvement of the caregiver may decrease problem behaviors in the care recipient); (Grade B, Level 2)
  - b) Support groups that focus on the management of behavioral problems and extend over several months; (Grade B, Level 1)
  - c) In-home systematic, comprehensive support by a health care provider with advanced training in dementia care over an extended period (i.e., couple of years); (Grade B, Level 1)
  - d) In-home psychoeducational intervention that teaches caregivers how to manage behavioral problems; (Grade B, Level 1)

- e) Non-pharmacological approaches to sleep disturbances can be effective for patients with AD but a combination of approaches will likely be required. (Grade B, Level 1)
25. Recommendations with regard to driving a motor vehicle and individuals with a mild to moderate dementia –
- a) Clinicians should counsel persons with a progressive dementia (and their families) that giving up driving will be an inevitable consequence of their disease. Strategies to ease this transition should occur early in the clinical course of the disease. (Grade B, Level 2)
  - b) No single brief cognitive test (e.g., MMSE) or combination of brief cognitive tests has sufficient sensitivity or specificity to be used as a sole determinant of driving ability. Abnormalities on cognitive tests such as the MMSE, clock drawing, and Trails B should result in further in-depth testing of driving ability. (Grade B, Level 3)
  - c) Driving is contraindicated in persons who, for cognitive reasons, have an inability to independently perform multiple instrumental activities of daily living (e.g. medication management, banking, shopping, telephone use, cooking) or any of the basic activities of daily living (e.g. toileting, dressing). (Grade B, Level 3)
  - d) The driving ability of persons with earlier stages of dementia should be tested on an individual basis. (Grade B, Level 3)
  - e) A health professional-based comprehensive off- and on-road driving evaluation is the fairest method of individual testing. (Grade B, Level 3)
  - f) In places where comprehensive off and on-road driving evaluations are not available, clinicians must rely on their own judgment. (Grade B, Level 3)
  - g) For persons deemed safe to drive, reassessment of their ability to drive should take place every 6 to 12 months or sooner if indicated. (Grade B, Level 3)
  - h) Compensatory strategies are not appropriate for those deemed unsafe to drive. (Grade B, Level 3)
26. Recommendations with regard to caregivers –
- a) The clinician should acknowledge the important role played by the caregiver in dementia care. The clinician should work with caregivers and families on an ongoing basis and schedule regular appointments for patients and caregivers together and alone. (Grade B, Level 3)
  - b) The clinician should: enquire about caregiver information and support needs; provide education to patients and families about dementia; and, assist in recruiting other family members and formal community services to share the caregiving role. If available refer patients to specialized dementia services (e.g., Alzheimer Society, community-based dementia programs, memory clinics) that offer comprehensive treatment programs including caregiver support, education, and training. (Grade A, Level 1)
  - c) The clinician should: enquire about caregiver health (both physical and psychiatric); offer treatment for these problems (including individual

- psychotherapy or medications as indicated); and, refer to appropriate specialists. (Grade B, Level 3)
- d) The clinician should enquire about problem behaviours of the dementia patient and the effect these behaviours are having on the caregiver. If these are causing significant caregiver distress, refer the caregiver and patient to specialized dementia services that can offer treatment to the patient and assist the caregiver in modifying their interactions with the patient. (Grade A, Level 1)
  - e) Pharmacotherapy for AD can decrease caregiver burden and the time required of caregivers to support the care-recipient. It should be considered as a means to help support caregivers. (Grade B, Level 1)
  - f) Future studies of medications for the treatment of AD and dementia should examine the impact of these agents on caregiver burden and the time required to support the care-recipient. There is a need to ensure consistency in the measurement of these outcomes. (Grade B, Level 3)
27. Recommendations with regards to education –
- a) All clinicians caring for patients with mild to moderate AD have to acquire the core knowledge and skills required to manage this condition (note: see recommendations 1, 13, 20, & 28 for specific educational needs of primary care physicians). (Grade B, Level 3)
  - b) A multifaceted educational program should be implemented to promote adoption of the recommendations of the 3<sup>rd</sup> CCCDTD by practitioners. (Grade B, Level 1)
28. Recommendations with regards to the organization and funding of care for those with a dementia –
- a) Every community should examine the services locally available for the management of those with a dementia, assess their adequacy, and implement plans to deal with identified deficiencies. (Grade C, Level 3)
  - b) There is a need to modify the prevailing model of chronic disease management (i.e., less reliance on promotion of patient self-management coupled with greater caregiver involvement) for dementia. The efficacy and efficiency of modified chronic disease management for dementia should be explored. (Grade C, Level 3)
  - c) Shared care models for the management of patients with mild to moderate AD and dementia should be developed and evaluated. This will require the acceptance of joint responsibility on the part of primary care practitioners and specialty services in delivering care to patients with dementia. (Grade C, Level 3)
  - d) Dementia care must to be adequately funded and reimbursed. Inadequate remuneration should not be a barrier to the delivery of good dementia care. (Grade C, Level 3)

## **Topic 6: Clinical practice guidelines for severe Alzheimer's disease**

1. Severe AD can be defined as the stage in which the patient becomes totally dependent on a caregiver for survival. This will typically correspond to MMSE <10 and GDS 6-7. (Grade B, Level 2)
2. Patients with severe AD should be assessed at least every four months or if treated with pharmacotherapy at least every three months. (Grade C, Level 3)
3. Assessment should include cognition (e.g., MMSE), function, behaviour, medical status, nutrition, safety and caregiver health. (Grade B, Level 3)
4. The goals for management are to improve the quality of life for patient and caregivers, maintain optimal function and provide maximum comfort. (Grade B, Level 3)
5. Medical management includes treatment of inter-current medical conditions (e.g., infections, parkinsonian symptoms, seizures, pressure ulcers), ameliorating pain, improving nutritional status and optimizing sensory function. (Grade B, Level 3)
6. Patients with severe AD can be treated with ChEIs, memantine or the combination. Expected benefits would include modest improvements in cognition, function and behavior and/or slower decline. (Grade A, Level 1)
7. Treatment with ChEIs and/or memantine should persist until clinical benefit can no longer be demonstrated. Treatment should not be discontinued simply because of institutionalization. (Grade C, Level 3)
8. The management of BPSD should begin with appropriate assessments, diagnosis, and identification of target symptoms and consideration of safety of the patient, their caregiver and others in their environment. (Grade B, Level 3)
9. Non-pharmacological treatments should be initiated first. Approaches that may be useful for severe AD include behavioural management for depression, and caregivers/staff education programs for a variety of behaviours. Music and multi-sensory intervention (Snoezelen) are useful during treatment sessions but longer-term benefits have not been demonstrated. (Grade B, Level 1)
10. Pharmacological interventions should be initiated concurrently with non-pharmacological approaches in the presence of severe depression, psychosis or aggression that puts the patient or others at risk of harm. (Grade B, Level 3)
11. Pharmacological interventions for BPSD should be initiated at the lowest doses, titrated slowly and monitored for effectiveness and safety. (Grade B, Level 3)
12. Attempts to taper and withdraw medications for BPSD after a period of three months of behavioural stability should occur in a standardized fashion. (Grade A, Level 1)

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13. Risperidone and olanzapine can be used for severe agitation, aggression and psychosis. The potential benefit of all antipsychotics must be weighed against the potential risks such as cerebrovascular adverse events and mortality. (Grade A, Level 1)
14. There is insufficient evidence to recommend for or against the use of trazodone in the management of non-psychotic, agitated patients. (Grade C, Level 3)
15. Benzodiazepines should be used only for short periods as p.r.n. agents. (Grade B, Level 1)
16. SSRIs can be used for the treatment of severe depression. (Grade B, Level 3)
17. If BPSD fail to improve after appropriate non-pharmacological and pharmacological interventions, refer to a specialty service. (Grade B, Level 3)

## **Topic 7: Management of dementia with a cerebrovascular component**

### **Use of non-pharmacologic interventions**

1. There is currently (as of March 2006) insufficient evidence to recommend the use of cognitive training for vascular dementia. (Grade C, Level 2)

### **Other therapeutic interventions**

2. Investigations for vascular risk factors. It is recommended that vascular risk factors are identified in all patients with vascular cognitive impairment. (Grade C, Level 3)
3. Treating hypertension. There is some evidence that treating hypertension may prevent further cognitive decline associated with cerebrovascular disease. There is no compelling evidence that one class of agent is superior to another; calcium channel blockers or ACE-inhibitors may be considered. (Grade B, Level 1) Treatment for hypertension should be implemented for other reasons, including the prevention of recurrent stroke. (Grade A, Level 1)
4. Antiplatelet therapy with aspirin. There is currently no evidence to support the use of aspirin to specifically treat dementia associated with cerebrovascular disease. (Grade C, Level 3) Aspirin or other antiplatelet therapies should be used for prevention of recurrent ischemic stroke in appropriate patients (AHA Guidelines, Stroke 2006). (Grade A, Level 1)
5. Nimodipine in vascular dementia. There is insufficient evidence for or against the use of Nimodipine for VaD. (Grade C, Level 1)
6. Use of memantine. There is some evidence of small magnitude of cognitive benefit that is not captured in global measures for patients with VaD. There is insufficient information to recommend memantine for the treatment of vascular dementia. (Grade C, Level 1).
7. Use of cholinesterase inhibitors in dementia due to combined Alzheimer's and Cerebrovascular Disease: There is fair evidence of benefits of small magnitude for galantamine in cognitive, functional, behavioral, and global measures in AD with CVD. Galantamine can be considered a treatment option for mixed Alzheimer's with Cerebrovascular Disease. (Grade B, Level 1)
8. Use of cholinesterase inhibitors in probable/possible vascular dementia using the NINDS-AIREN diagnostic criteria:
  - a) There is insufficient evidence for or against the use of galantamine; (Grade C, Level 1)
  - b) There is fair evidence of benefits of small magnitude for donepezil in cognitive and global outcomes, with less robust benefits on functional measures. Donepezil can be considered a treatment option for Vascular Dementia. (Grade B, Level 1)

## **Topic 8: Ethical issues in dementia**

### **Disclosure**

1. The process of diagnostic disclosure for persons with cognitive impairment or dementia must begin as soon as the possibility of cognitive impairment is suspected. (Grade A, Level 3)
2. Both the diagnosis of dementia and the disclosure of the diagnosis must be considered processes that provide opportunities for education and discussion. (Grade A, Level 3)
3. The potential for adverse psychological consequences must be assessed and addressed through education of the patient and family/caregivers. (Grade B, Level 3)
4. Once a diagnosis is established, this must be disclosed to the patient and their family/caregivers in a manner that is consistent with the expressed wishes of the patient. (Grade B, Level 3)
5. Follow-up plans must be made and discussed at the time of diagnostic disclosure. (Grade A, Level 3)

### **Consent for Therapy**

1. Provision of the best standard of care for the patient must always remain the priority. (Grade A, Level 3)
2. Drawing a clear distinction between research participation and clinical care is essential for both the patient and their family/caregiver. The distinctions between the clinician's role in the management of the individual's health care and his/her potential role in the conduct of research must be clearly understood by everyone, as must the procedures that represent standard care and research. In research settings, the availability of a physician other than the research physician to provide general care is recommended in order to ensure that decisions regarding treatment are made in the best interests of the patient. (Grade A, Level 3)
3. A diagnosis of dementia, or other forms of cognitive impairment, does not preclude competence to provide informed consent, whether it be for treatment decisions, for participation in clinical trials or for participation in non-therapeutic research. Competency must be considered as the ability to make an informed decision about participation in the particular context of the specific treatment or research study. (Grade A, Level 3)
4. For studies, it is reasonable to expect that the procedures that will be used to evaluate the ability of the potential subject to understand the nature of the research, the consequences of participation (i.e., potential risks and benefits) and alternative choices are described. However, at present there is insufficient evidence available to recommend the use of a specific standardized method for determining competency for decision-making either for treatment or research. (Grade B, Level 3)

5. Even in the absence of a legal determination of the competency of the patient with cognitive impairment or dementia, it is important that the clinician and researcher consider the consent process as one that should involve both the patient and their family/caregiver for treatment and research decision-making. In research settings, research ethics boards may explicitly require that consent/assent be obtained from both parties. (Grade B, Level 3)
6. The potential that competency for treatment and research decision-making will change over time must be recognized. This may lead to a change from one of obtaining the patient's ongoing consent to one of obtaining ongoing assent. Assent is almost invariably required, and the decision to discontinue treatment, whether it be therapy or research, must always be an option. (Grade A, Level 3)
7. To the best of their ability, clinicians and researchers must ensure that the decisions made by proxies regarding treatment and research are based on the prior attitudes and values of the patient. Proxies have a responsibility to represent the patient and all parties must recognize the challenges of doing so. (Grade A, Level 3)

## **Topic 9: Towards a Revision of Criteria for the dementias**

1. Although memory impairment is an important part of most dementias, there are some dementias (subcortical ischemic dementia, primary progressive aphasia, some other types of frontotemporal dementia) in which the requirement for memory impairment limits the sensitivity of a dementia diagnosis. The requirement for memory impairment should be dropped from the criteria for dementia, in favour of impairment in at least two domains of cognitive function.
2. There is no need to suggest that EEG and CSF studies help exclude a diagnosis of Alzheimer's disease.
3. There is no reason a priori to exclude patients younger than 40 or older than 90.
4. Broader use of the DSM-IV-TR category of "Dementia due to multiple etiologies" needs to be encouraged, with specification of the diseases contributing to the dementia routinely spelled out.
5. Revision of Alzheimer's disease criteria should recognize the possibility of focal presentations.
6. Depressive features should be recognized as concomitant in patients with Alzheimer's disease, and should not exclude a diagnosis.
7. Specific frontal temporal lobar degeneration criteria should be used, including criteria that recognize aphasic disorders, including primary progressive aphasia and semantic dementia, when these disorders are considered. At present, no one set of FTD criteria capture all the variants encountered in practice. The DSM-IV-TR category of "dementia due to Pick's disease" specifically is inadequate.
8. Given the present uncertainty with criteria for dementia with Lewy bodies, it is likely that the 2005 consensus criteria will need to be restricted to research environments. For now, the 1996 consensus criteria appear to be the most suitable for routine clinical practice.
9. Criteria for Parkinson's Disease Dementia are needed, and likely are best incorporated in new criteria which update those for dementia with Lewy bodies.
10. The proposal to develop new criteria for VCI has merit. The criteria should move away from the models of post-stroke dementia, and multi-infarct dementia. Moreover, they should emphasize opportunities for prevention of impairment that arises as a consequence of potentially modifiable cerebrovascular disease, even though cognitive impairment has been under-recognized as a manifestation of target organ damage.
11. The diagnosis of dementia due to normal pressure hydrocephalus should use the recent specific consensus criteria.
12. In young patients, or those with atypical presentations, systemic features or relevant risk factors, infectious causes should be borne in mind in the differential diagnosis of dementia. Focal cognitive deficits raise this

possibility, even when they do not meet traditional dementia criteria. Such features should prompt specialist referral.

13. Documentation of rapid progression should raise the possibility of Creutzfeldt-Jakob disease, and suggests prompt referral. The role of 14-3-3 protein detection requires further elaboration.

### **Note on authors:**

These recommendations all reached 80% or greater consensus at the CCCDTD3 meeting in Montreal , March 2006. The recommendations were prepared by the following working groups.

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