Recommendations for the Diagnosis and Treatment of Dementia 2012

Based on the Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDTD4) 2012

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Overview

Topics covered here:

- assessment and management of risk factor and primary prevention strategies
- Definitions and diagnostic criteria
  - criteria for MCI and dementias
  - biomarkers and amyloid imaging
- dementia screening in primary care
- specialist referral
- management of Alzheimer's Disease including new evidence on the indications and best use of drugs with special emphasis on discontinuation rules for cholinesterase inhibitors

Notation is made if the information presented here is part of previous (2007) recommendations or represent newer (2012) recommendations.

References

- Open Access publication as a supplement in *Alzheimer's Research & Therapy*
  - http://alzres.com/supplements/5/S1

- **Pharmacological recommendations for the symptomatic treatment of dementia: the Canadian Consensus Conference on the Diagnosis and Treatment of Dementia 2012**
- Nathan Herrmann, Krista L Lanctôt, David B Hogan *Alzheimer's Research & Therapy* 2013, **5**(Suppl 1):S5 (8 July 2013)

Overview - bottom line:

- In general, little practical change for most treating physicians in Canada.
- CCCDTD4 did not endorse a biomarker/PET/pre-symptomatic approach to diagnosis.
- Recommendations for individual treatment trials in most patients with Alzheimer's disease or Parkinson's Disease dementia, including those with concomitant vascular cognitive impairment, but not pure vascular dementia.

Background

Three earlier Canadian Consensus Conferences on the Diagnosis and Treatment of Dementia (CCCDTD)

Evidence-based recommendations on the diagnosis and treatment of Alzheimer's disease (AD) and related dementias.

Dissemination targeted to those who treat people with dementia, both primary care & specialist physicians (geriatricians, neurologists etc)

Background

4th CCCDTD convened in May 2012 in Montreal

Primary aim: to update the diagnostic approach to AD

In light of revised diagnostic criteria proposed by the International Working Group (IWG) and the recommendations made by the National Institute on Aging - Alzheimer Association workgroups (NIA/AA)

Methods

- Guided by the tenets of the AGREE.
- Note that prior CCCDTDs graded evidence using the Canadian Task Force on Preventive Health Care system
- CCCDTD4 mostly followed the GRADE system - in keeping with current recommendations for the conduct of consensus conferences.
- Evidence was graded both numerically by strength of recommendation (1 = strong, recommended; 2 = weak, suggested) and then alphabetically by quality of evidence (A = high, B = moderate, C = low)

Pre-conference

- Background articles (written by workgroups) were posted to a password protected website, accessible to conference participants
- Recommendations, modified where appropriate as a result of feedback, were posted for on-line voting.
- Organizations relevant to the care of people with dementia appointed delegates.
- Delegates had access to the background articles and could vote on recommendations.
- On-line voting closed May 03, 2012 (one day in advance of the conference assembly)

Conference

- Each topic briefly reviewed before voting on each recommendation.
- All participants (except for the 2 industry observers) were permitted to vote.
- In the event of failed consensus, on-line votes of conference participants not in attendance taken into account.

Consensus 2012

- Consensus defined as 80% or more of conference participants voting for the recommendation.
- Partial consensus defined as 60-79% of votes.
- Recommendations presented here reached consensus
- Full article with discussion of items that failed to reach consensus available

Rationale to re-evaluate Canadian criteria

- New criteria in the United States from the National Institute on Aging (NIA) and the Alzheimer Association (AA) would impact on Canadian practice
- Likewise, the International Working Group (IWG) proposed to diagnose AD **before dementia has become manifest**, using a new clinical phenotype ("memory impairment of the hippocampal type") and a biomarker
- The American Heart Association/American Academy of Neurology issued a statement about vascular contributions to cognitive impairment (VCI) and dementia.

Definitions/diagnostic criteria

probable/possible Alzheimer's disease dementia (2012)

Dementia is diagnosed when there are cognitive or behavioral (neuropsychiatric) symptoms that:

1. Interfere with the ability to function at work or at usual activities; and

2. Represent a decline from previous levels of functioning and performing; and

3. Are not explained by delirium or major psychiatric disorder;

4. Cognitive impairment is detected and diagnosed through a combination of

   (1) history-taking from the patient and a knowledgeable informant and

   (2) an objective cognitive assessment, either a "bedside" mental status examination or neuropsychological testing.

   Neuropsychological testing should be performed when the routine history and bedside mental status examination cannot provide a confident diagnosis.

Definitions/diagnostic criteria

probable/possible Alzheimer's disease dementia (2012)

5. The cognitive or behavioral impairment involves a minimum of two of the following domains:

   a. **Impaired ability to acquire and remember new information**––symptoms include: repetitive questions or conversations, misplacing personal belongings, forgetting events or appointments, getting lost on a familiar route.

   b. **Impaired reasoning and handling of complex tasks, poor judgment**––symptoms include: poor understanding of safety risks, inability to manage finances, poor decision-making ability, inability to plan complex or sequential activities.

   c. **Impaired visuospatial abilities**––symptoms include: inability to recognize faces or common objects or to find objects in direct view despite good visual acuity, inability to operate simple implements, or orient clothing to the body.

   d. **Impaired language functions** (speaking, reading, writing)––symptoms include: difficulty thinking of common words while speaking, hesitations; speech, spelling, and writing errors.

   e. **Changes in personality, behavior, or comportment**––symptoms include: uncharacteristic mood fluctuations such as agitation, impaired motivation, initiative, apathy, loss of drive, social withdrawal, decreased interest in previous activities, loss of empathy, compulsive or obsessive behaviors, socially unacceptable behaviors.

Definitions/diagnostic criteria VCI (2012)

Recommended (>80%)

Adoption of the criteria concerning for the 2011 ASA/AHA recommendations for the diagnosis of VCI.

Requires a demonstration of

1. the presence of a cognitive disorder by neuropsychological testing

2. a history of clinical stroke or presence of cerebrovascular disease by neuroimaging that suggests a link between the cognitive disorder and the vascular disease

Vascular Cognitive Impairment

VCI Diagnostic criteria

- The CCCDTD held in 2012 (*also known as "CCCDTD4"*), recommends the use of of criteria concerning VCI proposed by the NIA/AA working group in 2011, the core clinical criteria for which are as follows:
  - The presence of a cognitive disorder as determined by cognitive testing;
  - A recent stroke, or other brain blood vessel changes, where the severity and pattern of affected tissue are consistent with the types of impairment documented in cognitive testing.

Definitions/diagnostic criteria: DLB, PDD (2007)

- The clinical features of Dementia with Lewy bodies (DLB) and Parkinson disease dementia (PDD) often overlap.
- **DLB** should be diagnosed when this pattern of dementia occurs before or concurrently with parkinsonism.
- **PDD** can be diagnosed when there is well established PD followed by gradual onset of cognitive decline.
- **Alzheimer's disease** and **Lewy Body** frequently co-exist. Currently, it is not possible to offer guidelines that could separate the two diagnoses with a high specificity.

Assessment & management of risk, prevention strategies (2007)

Good evidence to recommend:

- Treating systolic hypertension (>160mm) in older individuals. The target BP should be 140mm or less
- avoiding the use of estrogens alone or together with progestins for the sole purpose of reducing the risk of dementia

Patterson C et al. **Diagnosis and treatment of dementia: 1. Risk assessment and primary prevention of Alzheimer disease.** CMAJ. 2008; 178(5): 548–556.

Assessment & management of risk, prevention strategies (2007)

Insufficient evidence for or against the following:

- The use of ASA and statin medications for the specific purpose of primary prevention of dementia
- Treatment of type 2 diabetes, hyperlipidemia and hyperhomocysteinemia for the specific purpose of reducing the risk of dementia
- The use of NSAIDs for the sole purpose of reducing the risk of dementia
- Supplementation with vitamins E or C for the prevention of dementia. (Grade C, Level 2) High dose vitamin E (≥400 units/day) is associated with excess mortality and should not be recommended.

Patterson C et al. **Diagnosis and treatment of dementia: 1. Risk assessment and primary prevention of Alzheimer disease.** CMAJ. 2008; 178(5): 548–556.

Assessment & management of risk, prevention strategies (2007)

Insufficient evidence, but physicans may consider the following:

- advocate for strategies including legislation, to reduce the risk of serious head injuries
- advise their patients about, and advocate for, appropriate protective clothing during administration of pesticides, fumigants, fertilizers and defoliants
- advocate for appropriate levels of education and strategies to retain students in appropriate learning environments.
- advise their patients about the potential advantages of increased consumption of fish
- higher levels of physical or mental activity as part of a healthy lifestyle, but not for the specific purpose of reducing the incidence of dementia

Patterson C et al. **Diagnosis and treatment of dementia: 1. Risk assessment and primary prevention of Alzheimer disease.** CMAJ. 2008; 178(5): 548–556.

Symptomatic treatments (2012)

Recommended: (>80%)

- As many cases of dementia have more than one contributing condition we recommend that management be based on those diagnoses that are believed to be the predominant contributing cause(s). (Grade 1B)
- Cholinesterase inhibitors are recommended as a treatment option for
  - Alzheimer's disease with cerebrovascular disease (Grade 1B)
  - dementia associated with Parkinson's disease (Grade 1A)
- A trial of a ChEI for most patients with AD as all three have demonstrated efficacy for mild to severe AD (Grade 1A)
  - Selection of which agent to use should be based on adverse effect profile, ease of use, familiarity, and differences between the agents in their pharmacokinetics and other mechanisms of action.

Cholinesterase Inhibitors in AD

ChEI are now recommended across the spectrum of severity in AD

Revised recommendations:

- All three ChEIs have demonstrated efficacy for mild to severe AD. A trial of a ChEI is recommended for most patients with AD. (Grade 1A)
- Direct comparisons do not suggest differences between ChEIs (Grade 2B). Selection of which agent to be used will be based on the 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.

Discontinuation of therapy (2012)

Revised recommendations

- Discontinuing ChEIs in patients with moderate to severe AD may lead to worse cognitive function and greater functional impairment as compared with continued therapy (Grade 2B). This effect must be balanced with the risk for known side effects and drug costs if therapy continues.

- ChEIs should be discontinued when:

Discontinuation of therapy (2012)

- (i) the patient and/or their proxy decision-maker decide to stop after being appraised of the risks and benefits of continuation and discontinuation;
- (ii) the patient refuses to take the medication;
- (iii) the patient is sufficiently nonadherent 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;
- (iv) the patient's rate of cognitive, functional and/or behavioral decline is greater on treatment compared with that prior to being treated;
- (v) the patient experiences intolerable side effects that are definitely or probably related to the ChEI;
- (vi) the comorbidities of the patient make continued use of the agent either unacceptably risky or futile (for example, terminally ill); or
- (vii) the patient's dementia progresses to a stage (for example, Global Deterioration Scale stage 7) where there would be no clinically meaningful benefit from continued therapy.

Discontinuation of therapy (2012)

- When a decision has been made to discontinue therapy because of a perceived lack of effectiveness, the dose should be tapered before stopping the agent and the patient should be monitored over the next 1 to 3 months for evidence of significant decline. If decline occurs, it is suggested consideration be given to reinstating therapy. (Grade 2C)

Symptomatic treatments (2012)

Recommended (>80%)

- A trial of an antidepressant *could* be considered if the patient has inadequate response to non-pharmocological interventions or has a major depressive disorder, severe emotional lability, or severe dysthymia (Grade 2A)
- Valproate should **not** be used for agitation and aggression in AD (Grade 1A)
- Risperidone, olanzapine and aripiprazole be used for severe agitation, aggression and psychosis associated with dementia where there is risk of harm to the patient and/or others (Grade 2A)
  - The potential benefit of all antipsychotics must be weighed against the significant risks such as cerebrovascular adverse events and mortality

Symptomatic treatments (2012)

Insufficient evidence for or against

- Combination therapy of a cholinesterase inhibitor and memantine – though this is thought to be rational and safe
  - *Revised recommendation* There is insufficient evidence to recommend for or against the combination of a ChEI and memantine (Grade 2B)
  - A previous recommendation holds: memantine is an option for patients with moderate to severe stages of AD. Use of memantine in mild stages of AD is not recommended
- the use of cholinesterase inhibitors and/or memantine for the treatment of neuropsychiatric symptoms as a primary indication (Grade 2B)
- the use of quetiapine in the management of severe agitation, aggression and psychosis associated with dementia (Grade 2B)
- the use of SSRIs or trazodone in the management of agitated patients (Grade 2B)

Behavioural and Psychological Symptoms of Dementia (BPSD)

- Think of non-pharmacological interventions first for BPSD
  - Triggers
  - Environment
  - Care schedules and approach
  - Identify opportunities for meaningful engagement, re-direction, distraction

Behavioural and Psychological Symptoms of Dementia (BPSD)

- Pharmacological management is complex
- Tool on Pharmacological Treatment of Behavioural Symptoms of Dementia in Long Term Care Facilities for Older Adults
  - Based on Canadian Coalition for Seniors Mental Health National Guidelines: www.ccsmh.ca
  - Dallas Seitz in collaboration with Mark Rapoport, Ken Le Clair, David Conn, Sudeep Gill, Kimberly Wilson

Tool on Pharmacological Treatment of Behavioral Symptoms of Dementia in Long Term Care Facilities for Older Adults

Based on:

Canadian Coalition for Seniors' Mental Health (CCSMH) National Guidelines: The Assessment and Treatment of Mental Health Issues in Long Term Care Homes

For more information or to order additional brochures, visit the Canadian Coalition for Seniors' Mental Health website: www.ccsmh.ca

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Canadian Coalition for Seniors' Mental Health

To promote seniors' mental health by connecting people, ideas and resources.

Coalition Canadienne pour la Santé Mentale des Personnes Âgées

Promouvoir la santé mentale des personnes âgées en reliant les personnes, les idées et les ressources.

Table 1: Medications for Agitation or Psychosis

Medication	Initial Dose	Titration & Maximum Dose	Formulations	Adverse Events	Comments
Atypical Antipsychotics					
Risperidone*	0.25mg BID or 0.5 mg OD	0.5mg every 3-7 days, 2mg max. total daily dose. May use 0.5 mg PO BID as prn	Tablet (0.25, 0.5, 1.0, 2.0 mg), oral dissolving, liquid, ointment, long-acting injection.	Most likely of atypicals to cause EPS	Best supported atypical antipsychotic for NPS
Olanzapine*	2.5mg QHS	2.5mg every 3-7 days, 10mg max. total daily dose. May use 2.5mg PO BID as prn	Tablet (2.5, 5.0, 7.5, 10.0 mg), oral dissolving, short-acting IM.	More sedating than risperidone or aripiprazole	Most likely to cause metabolic side-effects
Aripiprazole*	2mg PO OD	2-5mg every 3-7 days, max 10 mg total daily dose	Tablet (2.0, 5.0, 10 mg), short-acting IM.	Most likely to cause akathisia	
Quetiapine	12.5mg PO BID	12.5mg BID every 3-7 days to max. total daily dose of 200mg	Immediate & extended release formulations. (25,50, 100, 200mg, XR not available in 25 mg)	More sedating than a risperidone or aripiprazole	May be used for Parkinson's disease dementia or dementia with Lewy bodies at lower doses
Antidepressants					
Citalopram**	10mg PO OD	10mg every 1-2 weeks, max 20mg	Tablet, liquid forms	May cause hyponatremia	Best supported SSRI for NPS
Escitalpram**	5mg PO OD	5mg every 1-2 weeks, max of 10mg	Tablet	Same as citalopram	
Sertraline**	25mg PO OD	25mg every 1-2 weeks, max of 100mg	Tablet	Same as citalopram	
Anticonvulsants					
Carbamazepine	50mg PO OD	50mg every 1-2 weeks, given BID-QID, max. 500 mg	Tablet, liquid forms	Sedation, gait disturbance, neutropenia, hyponatremia	High potential to cause drug interactions, therapeutic drug level monitoring required
Typical Antipsychotics					
Haloperidol	0.5mg PO BID	0.5mg BID every 3-7 days, max 1.5mg BID	Oral, short-acting intramuscular, long-acting depot formulations	Most likely to cause EPS	May be used in emergency treatment where other IM medications are not available

Table 2: Medications for Sleep

Medication	Initial Dose	Titration & Maximum Dose	Formulations	Adverse Events	Comments
Lorazepam	0.25-0.5mg	0.5mg every 3-7 days, max 2 mg	Tablet, IM	Sedation, confusion	Short-term use only, tolerance may develop
Zopidone	3.75mg PO QHS	3.75mg every 3-7 days, max 15 mg	Tablet	Sedation, confusion	Short-term use only, tolerance may develop
Trazodone***	25mg PO QHS (sleep)	25mg every 3-7 days, max 100mg	Oral tablet	Sedation, orthostatic hypotension	Short-term use only for sleep For treatment of FTD may be given BID or TID doses

*For individuals who refuse oral medications, many medications can be crushed and mixed with food or liquids; olanzapine Zydis and risperidone solution can also be dissolved in some liquids. Contact a pharmacist to ensure compatibility. For severe physically aggressive behavior with a patients who will not take any medications by mouth, consider short-term use of intramuscular olanzapine or haloperidol depending on availability.

**May be used as first-line treatment for frontotemporal dementia

***May also be used in the treatment of frontotemporal dementia, see Special Populations section of this Pocket Card

Treatment Non-Response

- On average, approximately 10-20% of individuals will have a significant reduction in NPS with AA treatment (number needed to treat: 5 - 10).
- Initial improvement in NPS may occur relatively quickly with 24 hours of initiating AA therapy.
- Maximum benefit of a medication may take up to 2 – 4 weeks to be apparent
- For individuals who have little initial response to treatment within the first two weeks of treatment, consideration should be given to switching therapy.
- When changing medications for non-response, the first medication can be gradually tapered over 1 – 2 weeks and the new medication gradually increased.

Treatment Duration and Discontinuing Medications

- After symptoms have stabilized efforts should be made to reduce the dose of antipsychotics and discontinue if possible.
- Although the risk of mortality associated with antipsychotics is greatest initially after starting treatment, a persistent approximately two-fold increased risk of mortality is also observed with chronic treatment.
- Approximately 75% of individuals can be successfully taken off of antipsychotics without significant worsening of behavior.
- Successful discontinuation of antipsychotics is most likely for individuals who improved on low-doses of medication, individuals with less severe symptoms, and absence of sleep disturbance.

Special Populations

Dementia with Lewy bodies and Parkinson's Disease Dementia

- Individuals with Parkinson's disease dementia or dementia with Lewy bodies may be particularly susceptible to EPS with antipsychotics.
- Reductions in dopaminergic medications (e.g. levodopa or ropinirole) should first be attempted for psychotic symptoms in Parkinson's disease if possible.
- Cholinesterase inhibitors and memantine should be considered as first-line treatment for agitation, psychosis and aggression in these populations.
- Low dose quetiapine may be considered for significant psychosis, agitation or psychosis (starting dose 6.25 mg BID – gradually increased to a total of 100 – 150 mg daily as needed.

Frontotemporal Dementia (FTD)

- First-line treatments for FTD may include SSRI antidepressants such as citalopram or sertraline (see table 1).
- Trazodone may also be used to treat NPS in FTD starting at 25 mg PO BID/TID and gradually increasing as tolerated to a maximum of 100 - 300 mg daily.

Resources

CANADIAN:

Canadian Coalition for Seniors Mental Health: www.ccsmh.ca

Download free copies of the National Guidelines for The Assessment and Treatment of Mental Health Issues in Long Term Care Homes (Focus on Mood and Behaviour Symptoms)

Tool on the Assessment & Treatment of Behavioral Symptoms of Older Adults in Long Term Care Facilities

http://www.ccsmh.ca/en/projects/ltc.cfm

Tool on Depression: Assessment and Treatment for Older Adults

http://www.ccsmh.ca/en/projects/depression.cfm

Alzheimer's Knowledge Exchange:

Long Term Care:

http://www.akeresourcecentre.org/LTC

Murray Alzheimer Research & Education Program:

www.marep.uwaterloo.ca

INTERNATIONAL:

International Psychogeriatric Assocation

Behavioral and Psychological Symptoms of Dementia Education Pack

http://www.tpa-online.net/tpaonlinev4/main/programs/task/task_BPSD.html

ACKNOWLEDGEMENTS:

This pocket card was developed in collaboration with Drs. Nathan Herrmann, Mark Rapoport, Ken Le Clair, David Conn, Sudeep Gill, and Ms. Kimberley Wilson

Non-pharmacological Management

- Non-pharmacological management is key!
- Supports at home for patient and caregivers
- Safety considerations
  - Driving
  - Fire
  - Flood
  - Wandering
  - Firearms and dangerous occupations (e.g. powertools)
- Think of non-pharmacological interventions first for BPSD
  - Triggers, environment, re-direction/distraction

Community Resources

- Local Alzheimer Societies offer a variety of educational and support programs. A full list of provincial societies can be found at http://www.alzheimer.ca.
- Primary care physicians should familiarize themselves with local services for people with dementia and their families/carers including:
  - Alzheimer Society (in some provinces there is a First Link program via the Alzheimer Society in their region)
    - Education and support groups
    - Info Line
    - Wandering Registry
  - adult day programs
  - other community support programs
    - home care, meal assistance

For More Information

An online CME for physicians will be available in early 2013.

Check www.lifeandminds.ca for updates and a link to this.

Webinars aimed at the inter-professional health teams will be available in 2013 via the CDKTN.

Check www.lifeandminds.ca for updates and links to these.

Publications:

The main paper is available in the Canadian Journal of Neurological Sciences, Volume 39 Number 6 (Supplement 5) November 2012: *4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia*

Background articles are in press at Alzheimer Research and Therapy.

Check www.lifeandminds.ca for updates and links to these.