

Medications & Dementia



Winnipeg Regional
Health Authority

Office régional de la
santé de Winnipeg

Weighing the benefits versus risks

Dementia Care – March 4, 2019

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WRHA Long Term Care Program



Outline

- Medications for dementia
- Medications for behaviours associated with dementia
- Medications that can negatively affect cognition
- Other treatments for dementia – fact or fiction?



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Medications for Dementia



DEMENTIA

Defined: An 'umbrella' term used to describe the symptoms of a group of more than 100 conditions that impair memory, behaviours and thinking. The most common causes of dementia are outlined below.

Vascular dementia (VaD)

is the second most common form of dementia accounting for 20% of cases. VaD occurs through a reduced blood supply to the brain usually due to stroke.

Parkinsons disease (PD)

accounts for 5% of dementia cases. PD is a degenerative disorder of the central nervous system.

Alzheimers disease (AD)

is the **most common form of dementia** accounting for 50-70%. AD is a degenerative disease that attacks the brain resulting in impaired functioning.

Fronto-temporal dementia (FTD)

accounts for 5% of dementia cases. FTD is associated with rounded and tangled bundles of protein in brain nerve cells.

Dementia with Lewy bodies (DLB)

accounts for 15% of dementia cases. DLB is associated with Lewy bodies which are abnormal brain cells.

Medications for Cognition

- Target biochemicals in the brain which may be reduced by neuron loss
- Don't modify the underlying condition or it's progression
- Evidence for treatment of:
 - Alzheimer's disease
 - Dementia with Lewy bodies
 - Parkinson's disease dementia
- Not recommended for vascular or frontotemporal dementia

Medications for Cognition

- Cholinesterase Inhibitors
 - Cholinergic mechanism
 - Examples: donepezil, rivastigmine, galantamine
- N-methyl-d-aspartic acid (NMDA) Receptor Antagonist
 - Glutaminergic mechanism
 - Example: memantine

Cholinesterase Inhibitors



- Stabilizing or slowing progress of Alzheimer's Disease
 - Marked improvement 1 in 42
 - Minimal improvement 1 in 12
 - Cognitive stabilization 1 in 7
- Improvement in function and maintenance of independence hasn't been shown
- Modest benefit on cognition
 - Mean difference of 1.37 points on MMSE – minimum clinically important difference

Dementia: Bringing Evidence & Experience to Drug Therapy Decision Points; RxFiles; Oct 2014

*Dementia prevention, intervention and care.
The Lancet Commissions July 20, 2017.*

Side Effects



- Nausea, vomiting, diarrhea
- Weight loss, loss of appetite
- Muscle weakness or cramps
- Headache, dizziness
- Fatigue, drowsiness
- Urinary incontinence
- Increased sweating
- Vivid dreams or nightmares (donepezil)

Coverage

- Manitoba Pharmacare Program
 - Donepezil and galantamine moved to part 1 (full benefit) as of October 18, 2018
 - Exception Drug Status (EDS) submission no longer required
 - Cognitive tests (e.g. MMSE) should still be used for periodic monitoring
 - Rivastigmine is remaining in part 3 EDS
 - Prescriber needs to complete and submit the “*EDS Request Form – Cholinesterase Inhibitors*”
 - Person notified by letter if the request for coverage is approved or denied
 - Rivastigmine patch is not covered
- Private drug coverage plans may have different criteria

Cholinesterase Inhibitors

Medication	Doses	Form	Cost	Coverage
Donepezil	5 & 10 mg	Tablet	\$0.48 per tab	Pharmacare Part 1
	5 & 10 mg	Rapid dissolving tablet	\$3.62 per tab	Not covered
Galantamine	8, 16 & 24 mg	Extended release capsule	\$1.25 per cap	Pharmacare Part 1
Rivastigmine	1.5, 3, 4.5 & 6 mg	Capsule	\$1.30 per cap	Pharmacare Part 3 EDS
	2 mg/mL	Oral liquid	\$1.57/mL	Pharmacare Part 3 EDS
	4.6, 9.5, & 13.3 mg/24 hours	Patch	\$3.98/patch	Not covered

Lewy Body Dementia

- **Preferred:** Cholinesterase Inhibitors
 - Safe and well tolerated with a cognitive effect and a reduction in visual hallucinations
- **AVOID:** First generation (older) antipsychotics
 - Significant side effects including: sedation, rigidity, postural instability, falls, and increased confusion
- **CAUTION:** Second generation (newer) antipsychotics (e.g. low dose)

Memantine

- Moderate to severe Alzheimer's dementia (MMSE 3-14)
 - Small beneficial effect on cognition, activities of daily living and behaviour symptoms
- Mild to moderate Alzheimer's dementia
 - Marginal beneficial effect on cognition, no effect on behaviour or everyday functioning
- Benefit of combination with cholinesterase inhibitors?
 - Different mechanisms of action
 - Two consensus panels made “tentative positive recommendations”

Memantine

- Side effects:
 - Dizziness
 - Headache
 - Constipation
 - Confusion
- Not covered by Manitoba Pharmacare

Deprescribing



- **Deprescribing** means reducing or stopping medications that may not be beneficial or may be causing harm. The goal of deprescribing is to maintain or improve quality of life.
- Deprescribing involves patients, caregivers, healthcare providers and policy makers.
- **Deprescribing must always be done with the help of your doctor, nurse or pharmacist.**

Evidence-based Clinical Practice Guideline for Deprescribing Cholinesterase Inhibitors and Memantine



THE UNIVERSITY OF
SYDNEY



COGNITIVE
DECLINE
PARTNERSHIP
CENTRE

INSTITUT DE RECHERCHE

Bruyère 
RESEARCH INSTITUTE

- Contains seven recommendations that reflect the current evidence about when and how to trial withdrawal of cholinesterase inhibitors and memantine
- Emphasizes the need to consider the individual including their values, preferences and goals of care



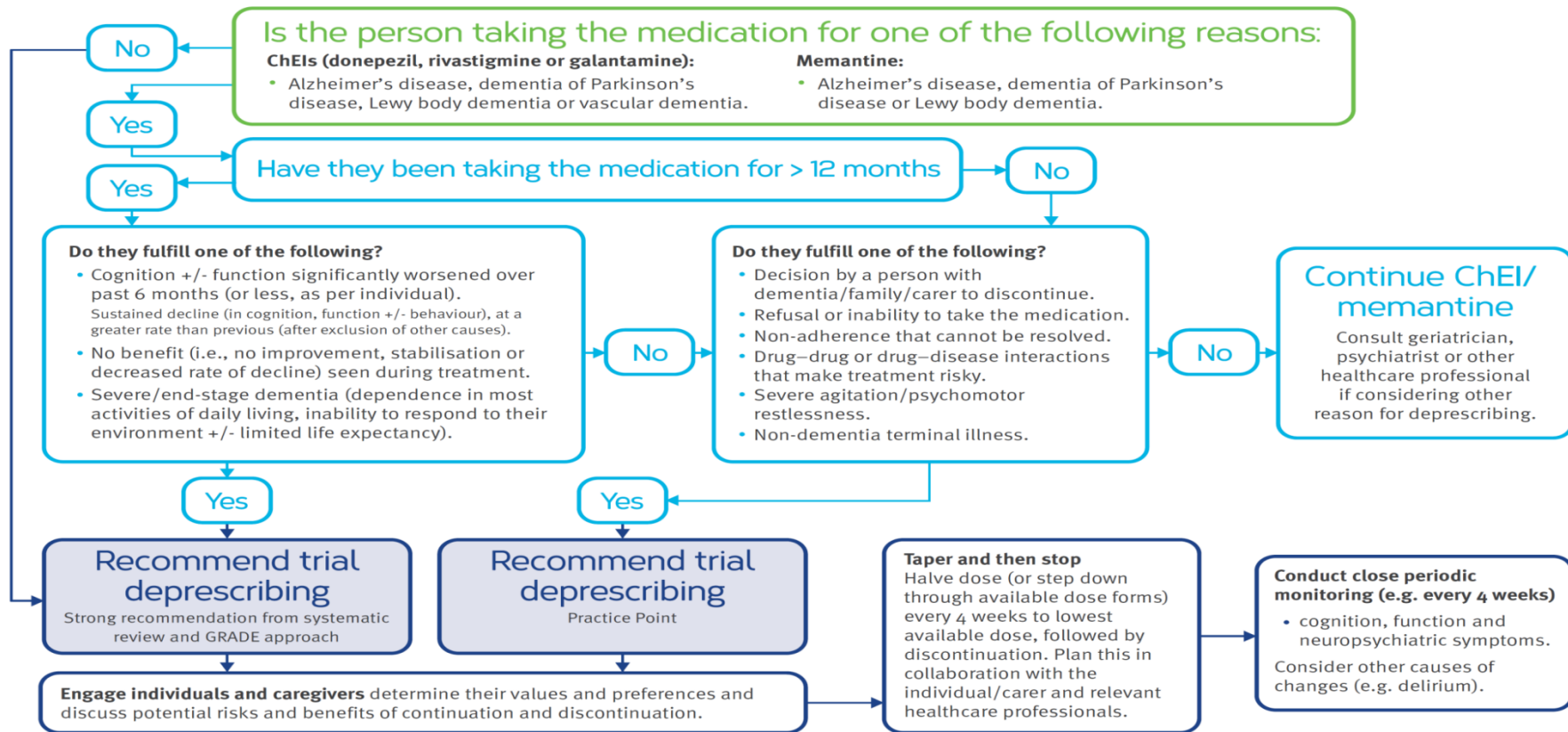
Deprescribing Cholinesterase Inhibitors & Memantine

- Individuals taking a cholinesterase inhibitor or memantine for Alzheimer's disease, dementia of Parkinson's disease, or Lewy body dementia for greater than 12 months, a trial discontinuation is recommended if:
 - Cognition and/or function has significantly worsened over the past 6 months
 - No benefit of improvement, stabilization or decreased rate of decline was seen at any time during treatment
 - Severe/end-stage dementia including dependence in most ADLs, inability to respond to their environment, and/or limited life expectancy

Strong recommendation; low evidence level

Deprescribing Cholinesterase Inhibitors & Memantine

- Trial deprescribing can also be considered:
 - Decision by a person with dementia and/or their family/carer to discontinue the medication
 - A person with dementia's refusal or inability to take the medication
 - Non-adherence that cannot be resolved
 - Drug-drug or drug-disease interactions that make treatment risky
 - Severe agitation/psychomotor restlessness
 - Non-dementia terminal illness





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Medications for Behaviours Associated with Dementia



1. Is a medication needed?

- Treat underlying causes of behaviour
 - Is there an unmet need?
 - Examples: pain, constipation, delirium
- Try non-medication therapy options first

2. Select appropriate medication based on symptoms

- Identify behaviour(s)
 - Medications should treat the specific behaviour(s)
- Decide whether possible benefits are likely to outweigh risks
- Start with a low dose and gradually titrate the dose as necessary or tolerated



Behaviour	Medication
Hallucinations, delusions, physical reactive behaviour, agitation (severe)	Antipsychotic
Agitation (severe) not responding to antipsychotics	Antidepressants e.g. citalopram or trazodone
Agitation (severe) in Lewy Body Dementia or Parkinson's	Cholinesterase inhibitor or low dose quetiapine
Anxiety (short term/intermittent)	Short-acting benzodiazepine like lorazepam before anxiety provoking events
Anxiety (chronic)	Antidepressant or anti-anxiety medication (e.g. buspirone)
Depression	Antidepressant
Mania / Bipolar	Mood stabilizer



Unlikely to Respond to Antipsychotics

Antipsychotics **do not help** to manage symptoms or behaviours like:




- Unsocial behaviour towards other people
- Apathy (no interest in what is happening)
- Inappropriate behaviour (like taking off clothes or sexual advances towards other people)
- Hiding or collecting things
- Repeating actions or words over and over
- Resistance to a specific person
- Wandering or being restless



Benefits & Harms: Antipsychotics

- When behaviours are severe and distressing, an antipsychotic trial may be reasonable
- At best, compared to placebo, antipsychotics resulted in targeted behaviour benefit in 1 out of 5 people treated
- Health Canada Advisory - 1.6 fold increase in mortality related to heart failure, sudden death or pneumonia. 1 extra stroke or death for every 100 people treated



 : Likely to be helped by antipsychotics
 : Likely to have no benefit from using antipsychotics
 : Likely to have a stroke or die*

Potential Side Effects

- More common:
 - Feeling sleepy or groggy
 - Confusion
 - Weight gain
 - High blood sugar or cholesterol
 - Dizziness caused by low blood pressure
 - Constipation
 - Swelling, usually around the ankles
 - Problems urinating (more common in older men)
 - Tight muscles that make the person shuffle or take short steps
- Less common:
 - Shaking in the hands or arms
 - Restlessness or needing to walk around a lot
 - Twitching face



Antipsychotic Options

- Haloperidol (Haldol®)
 - Useful for short term use in acute situations (e.g. psychosis or delirium)
 - Available in both oral and injectable dosage forms
- Risperidone (Risperdal®)
 - Only antipsychotic with Health Canada indication: *“short-term symptomatic management of aggression or psychotic symptoms in patients with severe dementia of the Alzheimer type unresponsive to non-pharmacological approaches and when there is a risk of harm to self or others.”*
 - Evidence of effectiveness for psychosis, agitation and physical reactive behaviours

Antipsychotic Options

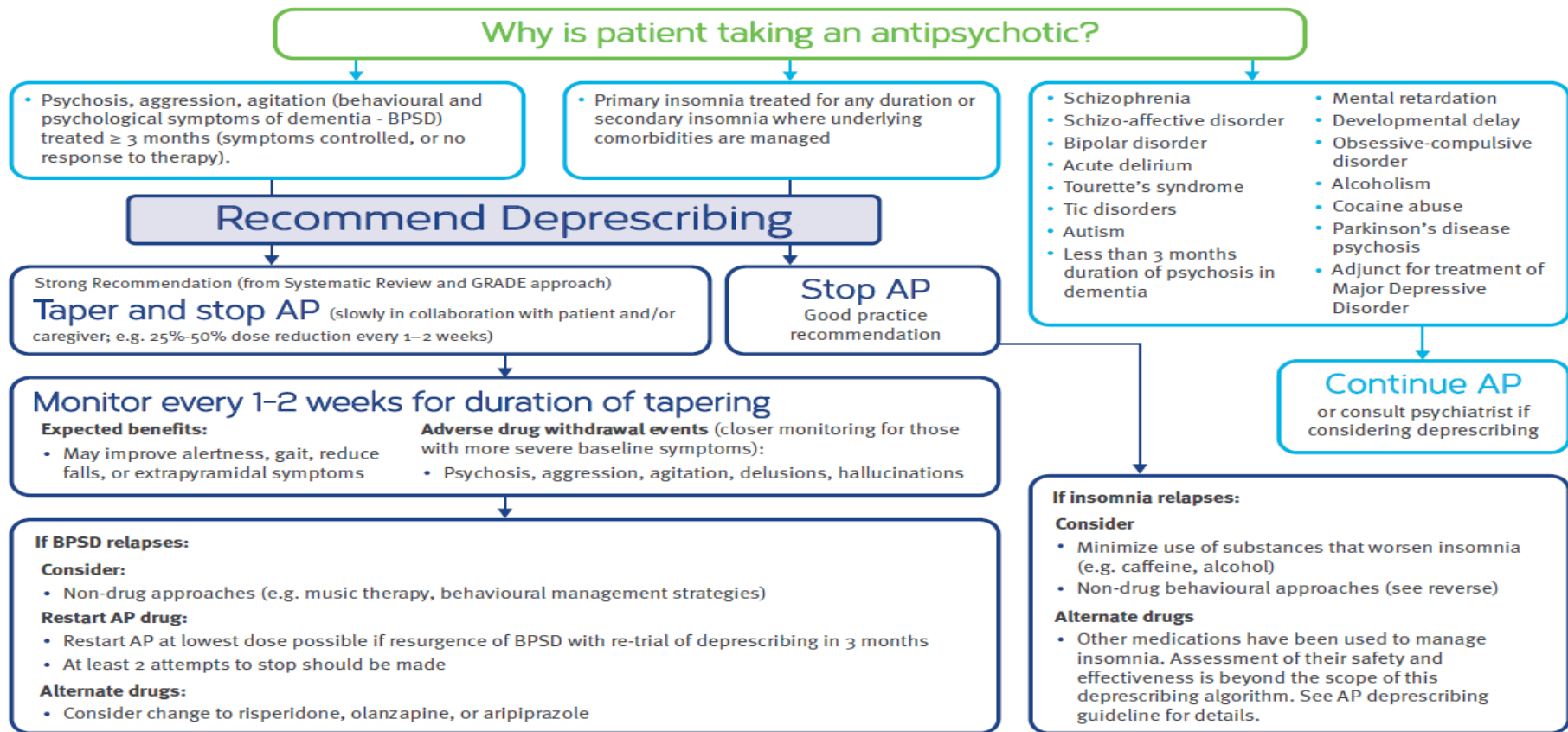
- Olanzapine (Zyprexa®)
 - Off-label use for behaviours in dementia
 - Evidence of effectiveness for agitation and physical reactive behaviours
- Aripiprazole (Abilify®)
 - Off-label use for behaviours in dementia
 - Evidence of effectiveness for agitation and physical reactive behaviours, but not psychosis
- Quetiapine (Seroquel®)
 - Off-label use for behaviours in dementia
 - Lacks evidence for effectiveness in agitation and physical reactive behaviours
 - No evidence for insomnia although use is increasing

Monitoring

- Assess over 1-3 weeks
- Effectiveness:
 - Frequency of symptoms
 - Severity of symptoms
 - Functional status (activities of daily living)
 - Quality of life
- Monitor side effects specific to the medication
- If lack of response and/or tolerability, adjust therapy
- Increase dose (if not at maximum) or taper/discontinue

Reassessment

- Consider dose reduction or discontinuation if the drug:
 - Is not effective
 - Has intolerable side effects or
 - Behaviours have been manageable and stable for 3-6 months
- Reassess after 3 months of antipsychotic use
 - Stopping or tapering antipsychotics may decrease “all cause mortality”
 - Behaviours may improve over time due to:
 - Disease progression, delirium resolution, adjustment to environment, effective non-medication strategies





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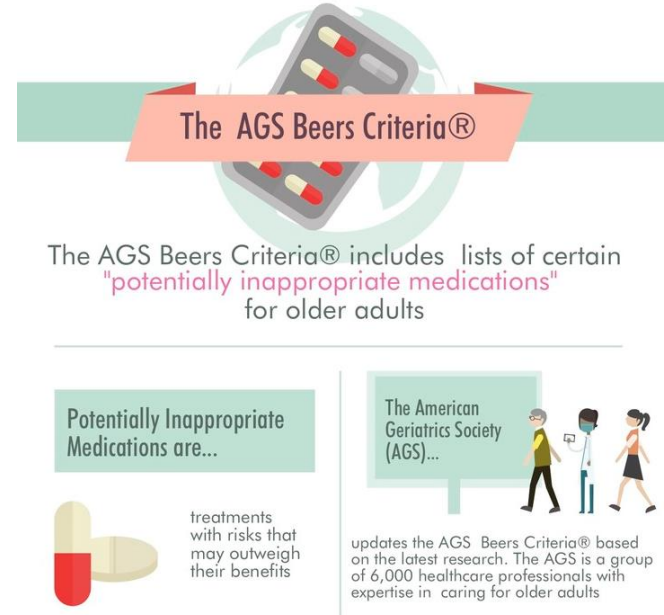
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Medications to Avoid



Medications that can negatively affect cognition

- The American Geriatrics Society publishes a list of potentially inappropriate medications for older adults – “Beers Criteria”
- These medications are identified as potentially inappropriate to prescribe to seniors due to:
 - An elevated risk of adverse effects
 - A lack of efficacy in older adults
 - Availability of safer alternatives



How many seniors in Canada are using potentially inappropriate medications?

- At least one claim for a drug on the Beers list → **49.4%**
- With claims for multiple drugs on the Beers list → **18%**
- Chronic users of 2 or more different drugs on the Beers list → **8.1%**
- Some of the most commonly used medication from the Beers List included:
 - Lorazepam
 - Amitriptyline
 - Quetiapine
 - Zopiclone
 - Oxazepam



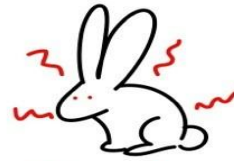
Anticholinergic Medications

- **AVOID:** Medications with moderate to high anticholinergic effects
 - Can reduce cognition
 - Can cause delirium
 - Reduces or negates the effects of cholinesterase inhibitors

Anticholinergic Effects

- Increased temperature
- Decreased sweating
- Increased heart rate
- Blurred vision
- Dry mouth
- Constipation
- Urinary retention
- Decreased cognition
- Delirium

ANTICHOLINERGIC SIDE EFFECTS



Hot as a hare



Dry as a bone

sketchymedicine.com



Blind as a bat



Red as a beet

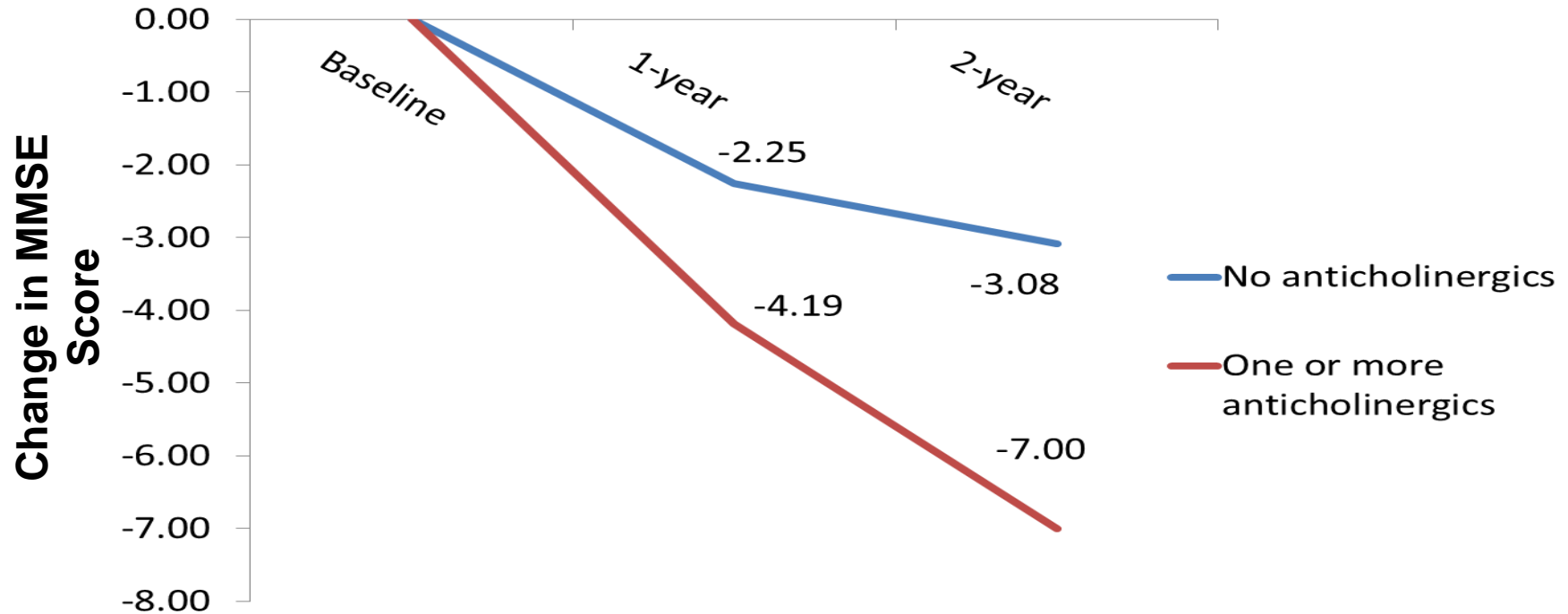


Mad as a hatter

Anticholinergic Medications

- **Antihistamines**
 - E.g. diphenhydramine (Benadryl[®], Nytol[®])
- **Antiemetics**
 - E.g. dimenhydrinate (Gravol[®])
- **Antispasmodics**
 - E.g. medications for overactive bladder (oxybutynin, tolterodine)
- **Antipsychotics** e.g. olanzapine
- **Antidepressants** e.g. amitriptyline, paroxetine

Effect of Anticholinergics on Cognition



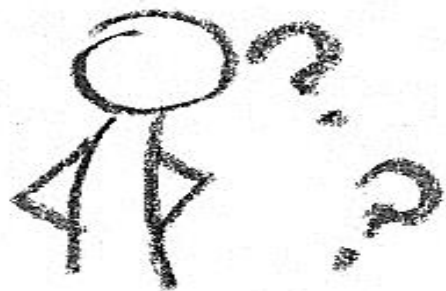
Lu C and Tune LE. *Am J Geriatr Psychiatry* 2003;11(4):458-61.



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Other Treatments for Dementia



fact or
fiction?

5p
CHEAPER THAN
THE DAILY MAIL
AND THE SUN
ANY DAY

DAILY EXPRESS

THE WORLD'S GREATEST NEWSPAPER express.co.uk



WEATHER: SHOWERS

TUESDAY AUGUST 14, 2012 50p

10p **DAILY EXPRESS**

**NOW MIGRANTS
MASS IN NEW
CAMP ACROSS
THE CHANNEL**



**FIVE STEPS
FOR DEM**

**Experts reveal
simple plan to
beat disease**

By Jo Wiley
A DAILY dose of cocoa could be the secret to halting Alzheimer's disease, researchers claim. Scientists have found that the potent ingredients in chocolate can dramatically improve cognitive impairment. Experts say pensioners should have some cocoa every day in a bid to keep dementia and Alzheimer's at bay. The key lies in health-boosting flavanols which are abundant in the sweet treat. Flavanols are an antioxidant also found naturally in fruit and vegetables such as grapes, berries and apple, drinks including tea and red wine, and other plant-based foods. Dr Giovanna Di Domenico, who headed the research team, said: "This study provides encouraging evidence that consuming cocoa flavanols as part of a calorie-controlled and nutritionally balanced diet could improve cognitive function. "Given the global rise in cognitive disorders, which have a huge impact on an individual's quality of life, the role of cocoa flavanols in preventing or slowing the progression of mild cognitive impairment to dementia warrants further research."



Aristocrat admits

**MURDERED TIA WRAPPED
IN A BLACK BED SHEET
AND PUT INSIDE A BAG**

SEE PAGE 7



**60MPH
STORMS
TO LASH
BRITAIN**

SEE PAGE 4

CHOCOLATE CAN HALT DEMENTIA

By Jo Wiley Health Correspondent

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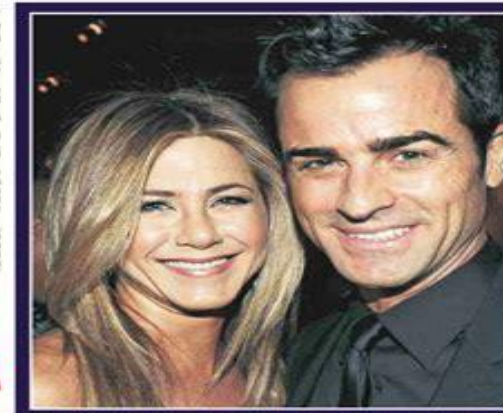
"Given the global rise in cognitive disorders, which have a huge impact on an individual's quality of life, the role of cocoa flavanols in preventing or slowing the progression of mild cognitive impairment to dementia warrants further research."

TURN TO PAGE 4



**ARLENE
PHILLIPS
REVEALS
DEMENTIA
ORDEAL**

SEE PAGE 31



SINGLE NO MORE: Jennifer Aniston is to marry the actor Justin Theroux

**JENNIFER
ANISTON
ENGAGED
...just a
few days
before
ex-hubby
Brad Pitt
marries
Angelina
Jolie**

SEE PAGE 9

EXPRESS

**GET A
TEACH
ODY...
FAST**

**GERMANY
ON TOP
OF THE
WORLD**

FOR EVERY READER

**BEAT
MER'S**

**CILLA
BLACK**
Why it's
not a
horra fun
getting
older

Blood Pressure & Dementia



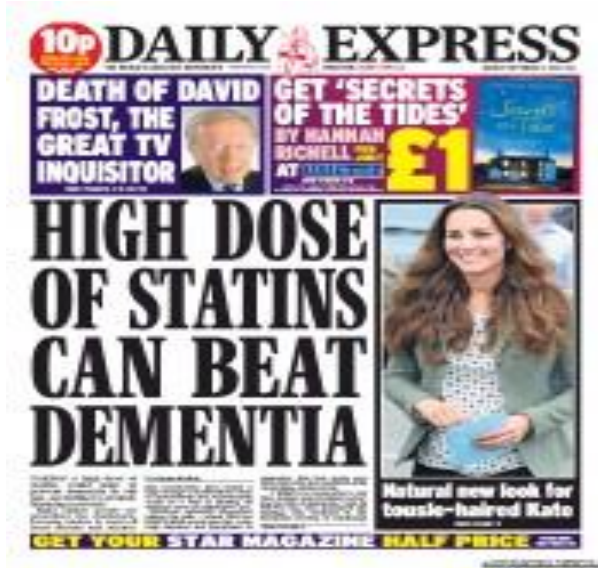
- **FACT** (partial)
 - Treatment of high blood pressure (hypertension) seemed to be important in the Prevention of Dementia by Intensive Vascular Care (preDIVA) trial
 - Need to weigh the benefits versus the risk of strict blood pressure control for people over 80 years

Vitamins & Dementia

- Vitamin E **FICTION**
 - Did not reduce incident dementia or have any effect on a range of secondary outcomes
- B Vitamins & folic acid **FICTION**
 - No significant effect on immediate memory over 6 months or global cognition



Statins & Dementia



- **FICTION**
- No interventional studies
- 1 observational study found statins did not affect cognitive decline in people with mild cognitive impairment

Ginkgo Biloba & Dementia

FICTION

“240 mg per day ginkgo biloba did not reduce the incidence of dementia, Alzheimer’s Disease, or cognitive decline over 6 years in high-quality trials”



Other Treatments

- Trials of other medications have not shown benefit in prevention or treatment of dementia:
 - Anti-inflammatory medications like naproxen, ibuprofen, celecoxib
 - Estrogen hormone-replacement therapy
 - Diabetes medication rosiglitazone



THE

TAKE-HOME MESSAGE

- Medications for cognition:
 - May be beneficial for Alzheimer's disease, Dementia with Lewy bodies and Parkinson's disease dementia
- Antipsychotic medications:
 - May be appropriate when behaviours are severe and distressing, but should be reassessed regularly
- Continue to weight the risks and benefits and consider deprescribing when appropriate



THE

TAKE-HOME MESSAGE

- Avoid
 - Medications that affect cognition like those with anticholinergic effects
- The other treatments for dementia in the headlines:
 - Often don't have any evidence of effect

Shared Decision Making

- Medication options should be discussed with the healthcare team before starting, changing or stopping a medication
 - *Has there been an adequate trial duration at an appropriate dose?*
 - *Effectiveness for symptoms*
 - *Are there side effects and are they manageable?*
 - *Discuss personal benefit and risk*
 - *Appropriate review and taper or discontinue*



Resources

Alzheimer Society of Manitoba: <https://alzheimer.mb.ca>

[Home](#)[About Us](#)[Upcoming Events](#)[Volunteer](#)[Contact Us](#)[DONATE](#)[A](#) [A](#) [A](#)

Drugs Approved for Alzheimer's Disease

Several medications are available that can help with symptoms such as decline in memory, language, thinking abilities and motor skills. Although there is currently no cure for the disease, those who respond to medication can experience improvements in their quality of life that may last for several years. People respond differently to treatments and not everyone will respond to these medications.

Mild to Moderate Alzheimer's Disease

Three drugs are available in Canada to treat symptoms in people with mild to moderate Alzheimer's disease:

1. [Aricept™](#) – Please note a warning from Health Canada reporting that Aricept™ may cause two rare but potentially serious conditions: muscle breakdown (rhabdomyolysis) and a neurological disorder called neuroleptic malignant syndrome (NMS). [Click here](#) to visit the Health Canada website for more details.
2. [Exelon™](#)
3. [Reminyl™](#) – Please note a safety alert from Health Canada reporting that Reminyl™ may cause a severe skin rash in some people. This rash is called Stevens-Johnson Syndrome and can be fatal. [Click here](#) to visit the Health Canada website for more details.

All are cholinesterase inhibitors. Cholinesterase inhibitors help by improving the ability of impaired nerve endings to transmit messages from one nerve cell to another. Depending on the medication, different side-effects may be experienced. These medications may be helpful for two to three years, possibly longer. Eventually, nerve endings degenerate to the point that medication is no longer helpful.

Moderate to Advanced Alzheimer's Disease

- [Ebixa®](#)
- [Aricept™](#)

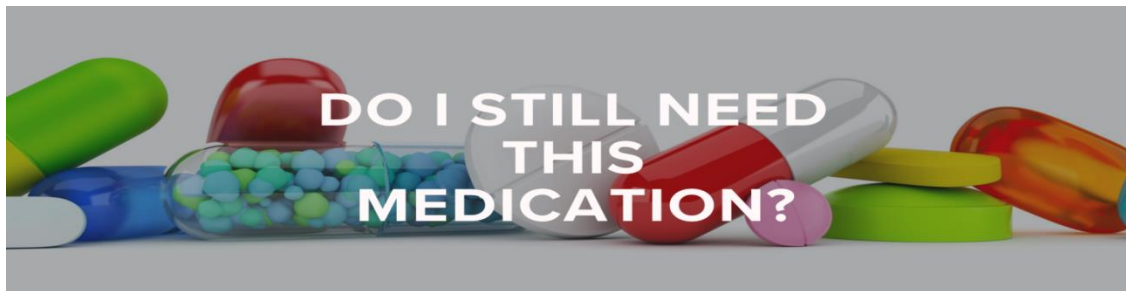
Resources

Canadian
Deprescribing
Network



Réseau
canadien pour
la déprescription

Public website: <https://www.deprescribingnetwork.ca/>



Health Professionals website: <http://deprescribing.org/>



deprescribing.org

Reducing medications safely
to meet life's changes

Moins de médicaments, sécuritairement –
pour mieux répondre aux défis de la vie

CARING
FOR HEALTH



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Resources

Use of Antipsychotics in Behavioural and Psychological Symptoms of Dementia (BPSD) Discussion Guide

This tool is designed to help providers understand, assess, and manage residents in LTC homes with behavioural and psychological symptoms of dementia (responsive behaviours), with a focus on antipsychotic medications. It was developed as part of Centre for Effective Practice's Academic Detailing Service for LTC homes. This tool integrates best-practice evidence with clinical experience, and makes reference to relevant existing tools and services wherever possible.

Important principles include:

- Being resident-centred,
- Being mindful of benefits, risks and safety concerns,
- Using an interprofessional team approach and validated tools,
- Prescribing conservatively, and,
- Reassessing regularly for opportunities to deprescribe medications that are no longer needed.

As always, efforts must be made to individualize any treatment decisions for the resident, with consideration given to caregivers, family members, as well as LTC staff.

Identify BPSD Symptom Clusters^{1,2}

Psychosis



Delusions
Hallucinations
Misidentification
Suspicious

Aggression



Defensive
Resistance to care
Verbal
Physical

Agitation



Dressing/undressing
Pacing
Repetitive actions
Restless/anxious

Depression



Anxious
Guilty
Hopeless
Irritable/screaming
Sad, tearful
Suicidal

Mania



Euphoria
Irritable
Pressured speech

Apathy



Amotivation
Lacking interest
Withdrawn

How Antipsychotic Medications are Used to Help People with Dementia

A Guide for Residents, Families, and Caregivers



Antipsychotic medications are used to treat a variety of different mental health conditions. They may be used to treat people with dementia when they have certain serious behaviours that are hard to manage with other strategies. As a member of the care team, you have an important role to play in helping the health care providers decide whether this treatment is a good choice for your family member or friend. This guide will help you learn more about how antipsychotic medications are used to help people with dementia.

Resources

Choosing Wisely Canada

<https://choosingwiselycanada.org/perspective/antipsychotics-toolkit/>



WHEN PSYCHOSIS ISN'T THE DIAGNOSIS

**A Toolkit for Reducing Inappropriate Use
of Antipsychotics in Long Term Care**

version 1.0

Treating Disruptive Behaviour in People with Dementia: Antipsychotic drugs are usually not the best choice

People with Alzheimer's disease and other forms of dementia can become restless, aggressive, or disruptive. They may believe things that are not true. They may see or hear things that are not there. These symptoms can cause even more distress than the loss of memory.

Health care providers often prescribe powerful antipsychotic drugs to treat these behaviours:

- Olanzapine (Zyprexa® and generic)
- Quetiapine (Seroquel®)
- Risperidone (Risperdal® and generic)

If you are uncertain if your loved one is taking one of these medications please ask their health care team.

In most cases, antipsychotics should not be the first choice for treatment, according to the Canadian Geriatrics Society. Here's why:

Antipsychotic drugs don't help much.

Studies have compared these drugs to sugar pills or placebos. These studies showed that antipsychotics usually don't reduce disruptive behaviour in older dementia patients.

Antipsychotic drugs can cause serious side effects.

Health care providers can prescribe these drugs for dementia for behavioural symptoms, but they cause serious side effects.

Side effects include:

- Drowsiness and confusion—which can reduce social contact and mental skills, and increase falls.



- Weight gain.
- Diabetes.
- Shaking or tremors (which can be permanent).
- Pneumonia.
- Sudden death.

Other approaches often work better.

It is almost always best to try other approaches first, such as the suggestions listed below.

Make sure the patient has a thorough exam and medicine review.

- The cause of the behaviour may be a common condition, such as constipation, infection, vision or hearing problems, sleep problems, or pain.
- Many drugs and drug combinations can cause confusion and agitation in older people.

Questions?



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