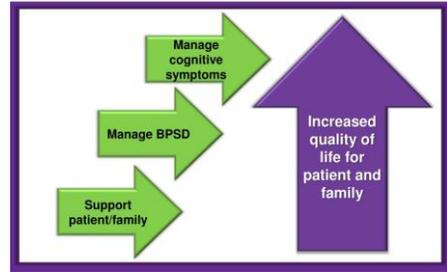




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Management of Alzheimer's Disease



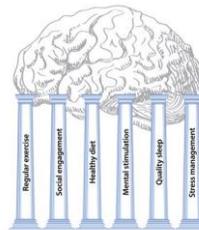
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Three Areas of Management

1. Family and social supports
2. Socialization and exercise
3. Cognitive enhancers

3

The 6 Pillars of Alzheimer's Prevention



Brain Health

What is good for prevention continues for treatment

- Exercise
- Social engagement
- Healthy diet
- Mental stimulation
- Quality sleep
- Stress management

4

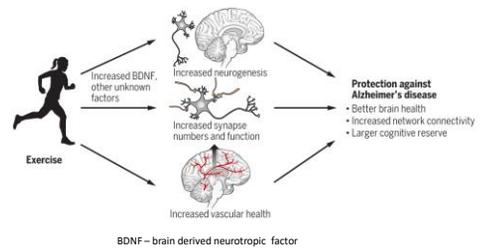
- According to the **Alzheimer's Research & Prevention Foundation**, regular physical **exercise** can reduce your risk of developing **Alzheimer's disease** by up to 50 percent.
- What's more, **exercise** can also slow further deterioration in those who have already started to develop cognitive problems.

<https://www.helpguide.org/articles/alzheimers-dementia-aging/preventing-alzheimers-disease.htm>

5

How might exercise protect against Alzheimer's disease?

Several pathways might explain how exercise protects the brain and prevents development of Alzheimer's disease. In mice, exercise enhances vascular health and increases the amount of BDNF in the brain, which promotes neurogenesis, survival of new neurons, and the formation of new synaptic connections.



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- The Benefits of **Socialization** for People Living with Dementia. Although interacting with people living with **Alzheimer's disease** or other forms of dementia can be challenging, especially for those who know them well, it can offer significant benefits.
- **Socialization** also seems to slow the progress of cognitive impairment

<https://www.waterstoneaugusta.com/importance-of-socialization-for-alzheimers-and-dementia-care/>

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CLINICAL PRACTICE GUIDELINES/CONSENSUS STATEMENTS

Recommendations of the 4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCCDT4)

Serge Gauthier, MD, Christopher Patterson, MD, Howard Chertkow, MD, Michael Gordon, MD, Nathan Herrmann, MD, Kenneth Rockwood, MD, Pedro Rosa-Neto, MD, PhD, Jean-Paul Soucy, MD on behalf of the CCCDT4 participants*

McGill Center for Studies in Aging, Montreal, QC
DOI: <http://dx.doi.org/10.5770/cji.15.49>

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Treatment Recommendations from CCCDTD4

- All three cholinesterase inhibitors of demonstrated efficacy for mild to severe Alzheimer disease
- No good evidence to recommend for or against use of ChEI and/or memantine for the treatment of neuropsychiatric symptoms

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Treatment Recommendations from CCCDTD4

- Discontinuing ChEI in patients with moderate to severe Alzheimer disease may lead to worsening of cognitive functioning and functional impairment.
- Taper dose of ChEI and monitor over one to three months.

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Cholinesterase Inhibitors:

Donepezil (Aricept), Galantamine (Reminyl), Rivastigmine (Exelon)

N-Methyl D-Aspartate (NMDA) Antagonist:

Memantine (Ebixa)

ChEI

Late 1990's
 Cholinergic deficit in AD
 Inhibit Acetyl-cholinesterase and Butyryl-cholinesterase
 Mild to moderately severe AD:
 • Donepezil (5 mg, 10 mg)
 • Galantamine (8 mg, 16 mg, 24 mg)
 • Rivastigmine (3 mg BID, 6 mg BID)
 Start at lower dose and increase after 4 weeks
 Main side effects are nausea, diarrhea, anorexia, runny nose, runny...everything

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DONEPEZIL FOR ALZHEIMER'S — META ANALYSIS

Donepezil for dementia due to Alzheimer's disease (Review)

Birks JS, Harvey RJ

28 studies, 8257 participants
 - June 2018

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DONEPEZIL FOR ALZHEIMER'S - META ANALYSIS

Donepezil

- Mild improvement in cognitive scores and functional scores
- No improvement in behaviour
- Discontinued due to adverse events in 5-10%, about 27% have an adverse event
- No additional functional benefit greater than 10 mg
- No benefit below 5 mg
- Not much difference between 5 mg and 10 mg

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PRAGMATIC CLINICAL TRIAL

Campbell, N.L. et al

J Am Geriatr Soc 65:1497-1504, 2017

196 participants, memory clinics, 18 weeks

50% discontinued therapy

- 58% adverse event
- Cost
- Forgot, lost prescription, etc.

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CHOLINESTERASE INHIBITORS IN ALZHEIMER'S

Caution:

- Bradycardia
- Bronchospasm
- Bleeding peptic ulcer
- Prolonged QTc
- Seizures
- Anorexia, low body weight, diarrhea
- (Advanced age)
- Unreliable delivery system

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ALZHEIMER'S

Rivastigmine:

- Small effects
- All studies funded by Novartis

Galantamine:

- Cochrane review 10 trials, 6800 participants
- Mild changes in cognition and function
- No change in behaviour
- Some improvement in MCI but excess death rate

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NO BENEFIT OF COGNITIVE ENHANCERS

Frontotemporal dementia

- Pick's
- ALS associated

Alcohol-related dementia

Vascular dementia (improves testing, higher rate of side effects)

Mild cognitive impairment (MCI)

Delirium

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Cochrane Database of Systematic Reviews

Memantine for dementia

Cochrane Systematic Review - Intervention | Version published: 20 March 2019

- Small clinical benefit of memantine in people with moderate-to-severe AD, which occurs irrespective of whether they are also taking a ChEI
- no benefit in people with mild AD.

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Cochrane Database of Systematic Reviews

Memantine for dementia

Cochrane Systematic Review - Intervention | Version published: 20 March 2019

- Small clinical benefit of memantine in people with moderate-to-severe AD, which occurs irrespective of whether they are also taking a ChEI
- No benefit in people with mild AD
- Clinical heterogeneity in AD makes it unlikely that any single drug will have a large effect size

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Dementia	Donepezil	Galantamine	Rivastigmine	Memantine
Alzheimers	✓ mild, moderate	✓ mild, moderate	✓ mild, moderate	✓ moderate severe
Vascular	?	✓	?	?
Lewy Body	✓	✓	✓	✓
Fronto-temporal	No	No	No	No

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Cholinesterase Inhibitors

PRECAUTIONS

- Pre-existing bradycardia
 - Severe liver disease
 - Peptic ulcer disease
- Current alcoholism
 - Asthma
 - COPD

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The Assessment of Cardiac Status Before Prescribing Acetyl Cholinesterase Inhibitors for Dementia

Version number: 1

First published: April 2016

Prepared by: Yorkshire & Humber Clinical Networks

Review date: October 2017

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- no compelling evidence that undertaking a routine ECG in all patients prior to initiation of AChEIs was either justifiable or effective
- AChEIs can induce sinus bradycardia, sino-atrial block, and aggravate pre-existing sinus node disease and atrioventricular block
- small, but significant risk of causing bradycardia
- QT prolongation appears to be a rare side effect; potential however for fatal arrhythmias in those with a significant QT prolongation, particularly those with a co-morbid hypo/hyperkalemia
- Patients who should have an ECG are:
 - Unexplained syncope
 - Bradycardia
 - Patients taking concomitant cardiac rate-limiting medication
e.g. beta-blockers, amiodarone

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**DECISION TREE**

1. Confirm diagnosis
2. Memory enhancers are not effective in Mild Cognitive Impairment
3. Review side effects and precautions
4. Get an ECG
5. Follow-up appointment for a prescription

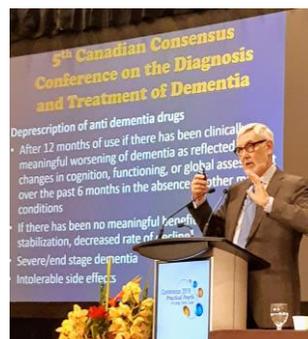
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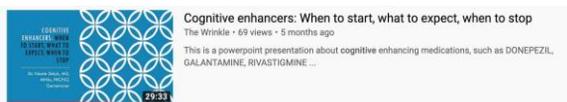
DECISION TREE

- Reassess in 4 – 6 weeks
- Assess for side-effects and increase dose
- Reassess at three months, adjust dose
- Repeat cognitive testing in 6 to 12 months

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YouTube

COGNITIVE ENHANCERS
When to Start and When to Expect to Stop

Dr. Nicole Didyk



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