Dementia Management in Primary Care

Arlene Kelly-Wiggins MD CCFP (COE) Day In Family Medicine January 2024

Disclosures

No competing or conflicting interests

Founding Member and Current Advisory Role with CBU Centre for Excellence in Healthy Ageing

Principal Investigator in CB for Goal Attainment Study with Ardea Outcomes

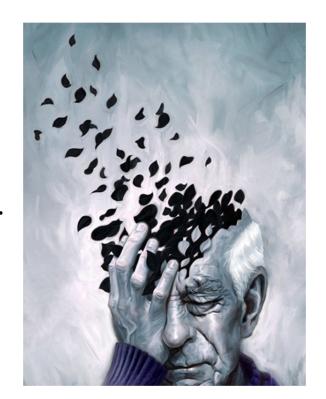
Objectives

At the conclusion of this presentation, participants will be able to:

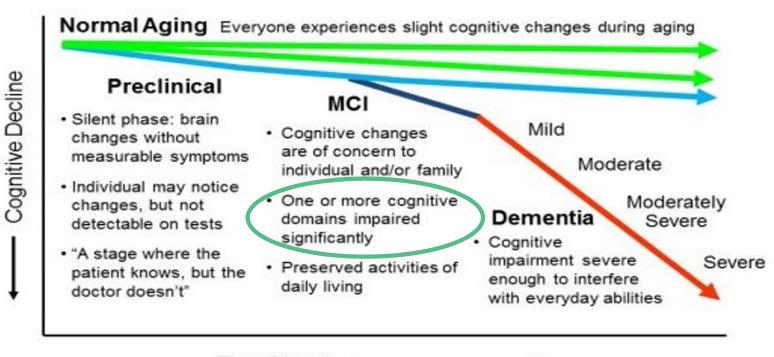
- Understand the role of diagnostic testing and memory assessment in the context of a dementia differential diagnosis.
- Differentiate between various acetylcholinesterase inhibitors and their respective roles when creating a treatment plan.
- Understand the role of geriatric specialists when managing complex cases of dementia and coordinating holistic care.

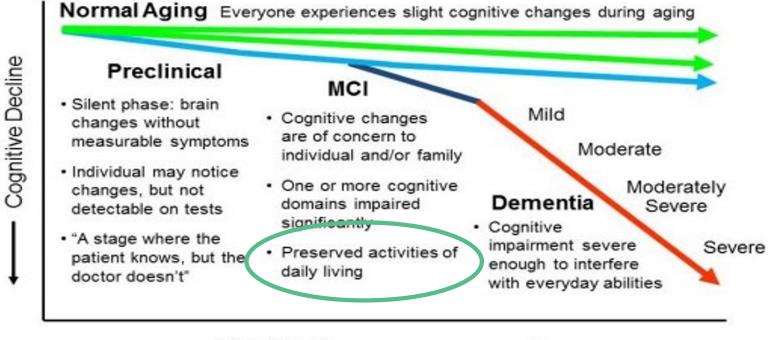
Working Definition: Dementia

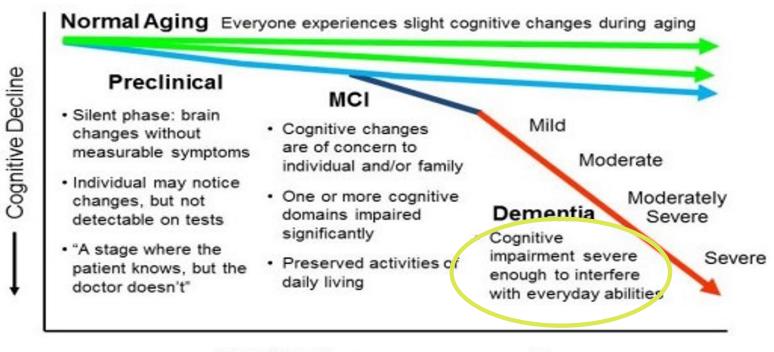
A **decline in cognitive function** severe enough to **interfere with independence** in daily activities.



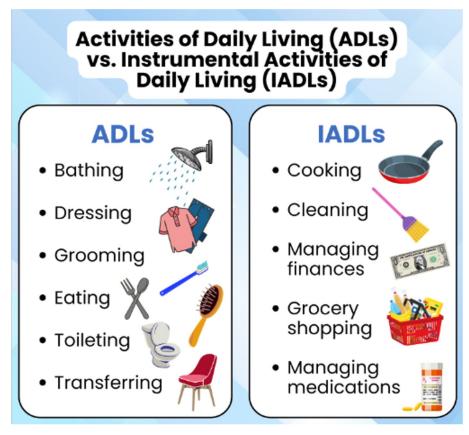
Normal Aging Everyone experiences slight cognitive changes during aging Cognitive Decline Preclinical MCI · Silent phase: brain Mild · Cognitive changes changes without are of concern to measurable symptoms Moderate individual and/or family · Individual may notice · One or more cognitive Moderately changes, but not Dementia domains impaired Severe detectable on tests significantly Cognitive · "A stage where the impairment severe Severe · Preserved activities of patient knows, but the enough to interfere daily living doctor doesn't" with everyday abilities







Assessing Function - BADLs/IADLs



Dementia Assessment

- 92% Dx made by Hx + Px, improved accuracy with collateral
- No evidence for screening at population level
- Ask about and document change in function BADLs + IADLs
- Assess for and treat other medical conditions, delirium, depression
- Recommended Investigations:
 - CBC, Lytes, Cr, Hgb A1c, random glucose
 - TSH, B12, CRP
 - ?Imaging

When to Image?



- Most guidelines recommend CTH at minimum
- Age <60 y
- Rapid decline (<1-2 months)
- Recent head trauma
- CNS symptoms headache, seizures, lateralizing/localizing features, abN gait
- PMHx malignancy
- Anticoagulation/bleeding disorder
- Unusual cognitive Sx aphasia
- Urinary incontinence + gait disturbance
 - o ?NPH

MRI in more concerning presentations, younger people, atypical symptoms, rapid progression - request coronal views through hippocampus

Cognitive Testing

Mini-Mental State Examination (MMSE)

Patient's Name:	Date:

Instructions: Score one point for each correct response within each question or activity.

Maximum Score	Patient's Score	Questions
5		"What is the year? Season? Date? Day? Month?"
5		"Where are we now? State? County? Town/city? Hospital? Floor?"
3		The examiner names three unrelated objects clearly and slowly, then the instructor asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible.
5		"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65,) Alternative: "Spell WORLD backwards." (D-L-R-O-W)
3		"Earlier I told you the names of three things. Can you tell me what those were?"
2		Show the patient two simple objects, such as a wristwatch and a penci and ask the patient to name them.
1		"Repeat the phrase: "No ifs, ands, or buts."
3		"Take the paper in your right hand, fold it in half, and put it on the floor. (The examiner gives the patient a piece of blank paper.)
1		"Please read this and do what it says." (Written instruction is "Close your eyes.")
1		"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)
1		"Please copy this picture." (The examiner gives the patient a blank piace of paper and asks himiher to draw the symbol below. All 10 angles must be present and two must intersect.)
30		TOTAL

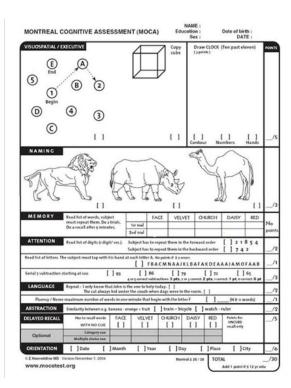
MMSE

- Orientation, memory, attention, language and visuospatial
- Brief, repeatable
- Language/culture sensitive
- No assessment of executive function or visual memory
- Lower sensitivity
- Education affects performance
- Cutoff 24/30

Cognitive Testing

MoCA

- Developed to overcome limited sensitivity of MMSE
- Includes visuospatial and executive function assmt
- Differentiates MCI from dementia
- MoCA w/i 4 or 5 pts of MMSE = normal
- Cutoff 21-22/30



Cognitive Testing

MoCA

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Cutoff 21/30-22/30

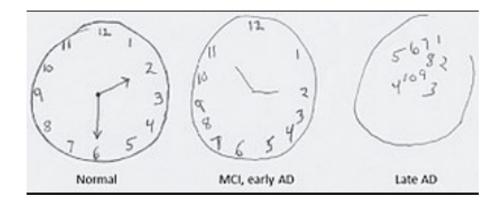
Generally 4-5

Concern re: training requirements - clinic can sign disclaimer at mocatest.org

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ATTENTION	Read list of digits (1 dig			peat them in t			[]211	8 5 4	
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Read list of letters. I	ne subject must rap with			CWINNEY	LUATA			FAAD	_
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Serial 7 subtraction LANGUAGE Fluency / Nam ABSTRACTION	starting at 100 [Repeat: I only know th The cat alway e maximum number of w Similarity between e.g.	at John is the rs hid under the ords in one mi banana - oran	e geomet subtra one to help to he couch when insite that beg nge = fruit [ections: 3 pts, 2 ectay. [] n dogs were in in with the lett] train – bic	the room. [er f ycle []	pts, coor	(N ≥ 11 w	riech O pt	

Mini-Cog

- 3 words BALL, CAR, MAN
- Clock drawing test
- Score 1, 2, or 3 for recall
- Score 0 or 2 for clock
- Positive screen < 3/5
 - Will prompt further testing
- Negative screen ≥ 3/5
 - Cannot rule out dementia



Normal = all numbers present, in order, correct hand placement (11:10) - 2/2

Abnormal - 0/2

Diagnosis



Clinical Diagnosis

- Based on Hx + collateral information, cognitive testing, physical exam
- Consider the earliest and most prominent impairment Domains of Cognition



New Learning and Memory:

On History:

- Repetitiveness
- Misplacing objects
- Forgetting appointments and dates
- Any "red flag" events (e.g. leaving the stove on)

On Testing:

- Impaired recall not responsive to cueing i.e., impaired registration
- Impaired orientation
- Attention is usually intact

Most likely Dx:

Alzheimer's Dementia

Treatment is ChEI, and treat comorbid mood D/O



Visuo-Spatial:

On History:

- Getting lost in familiar surroundings
- Difficulty recognizing objects/faces
- Blurry vision, normal eye exam, difficulty reading, many pairs of glasses
- Can't align objects, cannot stack or replace objects
- Visual hallucinations, mis-interpretations

On Testing:

- Impaired copying, construction, and clock-drawing
- Unable to do Trails

On Exam:

- Parkinsonism, stooped + shuffling gait, tremor, masked facies
- Obvious coordination impairments -

Most likely Dx:

Lewy Body Dementia or Posterior Cortical Atrophy (PCA - variant of AD)

Both conditions warrant trial ChEIs - LBD often responds quickly but not sustained



Attention:

On History:

- Distractible
- Cannot follow TV shows, movies, conversations
- Repetitive questions but within seconds/minutes

On Testing:

- Impaired/inconsistent word registration
- Cannot spell backwards or do reverse digit span, reverse days of week
- Difficulty attending to/staying on task at hand

Most likely Dx:

- Acute change: think delirium
- Fluctuating attention/cognition also associated with DLB
- Anxiety and depression also affect attention
- Attention is usually intact in mild-mod AD



Language

On History:

- Substituting words:
 - Phonemic sound alike
 - Semantic close in meaning/function
- Difficulty with names of people/objects
- Prominent word-finding pauses
- Filler words whatshisname, whatchamacallit

On Testing:

- Difficulty with naming objects
- Low letter/category fluency
- Impaired pronunciation

Most likely Dx:

Primary Progressive Aphasia (PPA)



Primary Progressive Aphasia (PPA) Subtypes:

- Logopenic AD variant impaired repetition, prominent word-finding difficulties
- Semantic FTD variant empty speech, word salad
- Non-Fluent, agrammatic FTD variant
 halting speech, cadence is "off"

Often improvement with SSRIs, logopenic variant is treated with ChEIs

Semantic variant usually has behavioural component and more rapid decline



Executive Function

On History:

- Difficulty at work learning new systems
- Trouble planning, multitasking, or with judgement
- Impulsivity or restlessness
- New apathy, loss of initiative

On Testing:

- Impaired clock construction, planning, abstracting time
- Impaired Trails and sequencing tasks, set-shifting

Most likely Dx:

Vascular Cognitive Impairment/Vascular Dementia

Symptoms usually respond to SSRIs, often we offer ChEI trial, galantamine has some evidence



Social Cognition

On History:

- Younger age, <65 y, onset in 40s-50s
- New and concerning behavioural changes
- Often cognition intact
- Impulsive, substance use, hyperorality, hypersexual behaviours
- Table manners often first to go
- Often Dx'd with psychiatric conditions before dementia Dx'd

On Testing:

- Recall, orientation, visuospatial tasks intact testing can be "normal" for years
- Impaired judgement + insight
- Disinhibited "F" words

Most likely Dx:

Behaviour Variant Frontotemporal Dementia (bvFTD)

Manage Sx/behaviours with SSRIs, family education

Initial Symptoms	Cognitive Domain	Most Likely Dx	Treatment
Repetitiveness, forgetfulness, misplacing objects, not oriented to time, "amnestic"	New learning and memory	Alzheimer's dementia	Cholinesterase inhibitors
Impaired organization, unable to plan or multi-task, new apathy, loss of interest	Executive function	Vascular dementia	SSRIs
Decline in social graces, behavioural changes, impulsivity, hyper-sexuality, <60y	Social cognition	bvFTD	SSRIs, family interventions
Distractible, unable to focus, fluctuating cognition	Attention	Acute change: ?delirium	Identify and treat cause
Wordfinding, non-fluent speech, empty speech, anomia, acalculia	Language	PPA - semantic, logopenic, non- fluent	Logopenic - ChEl Others - SSRIs
Getting lost, not recognizing faces, objects, % vision changes, changes in hand-eye coordination	Visuospatial	PCA - AD variant DLB - often w VH +/- PD Sx	ChEls

Staging According to Impairment: CURE + IRAN

STAGE	CURE (COGNITION)	IRAN (FUNCTION)
MILD	CURRENT EVENTS (news, sports, weather, etc)	IADLs (higher order functions)
MODERATE	US PRES/CAN PM (major figures)	REWEARING (personal care)
SEVERE	RELATIVES (forgetting names + relationships)	ADLs (personal care)
VERY SEVERE	EVERY ASPECT OF MEMORY/COGNITION	NON-VERBAL, NON- AMBULATORY

Pharmacological Therapy

Mainstay of AD treatment is cholinesterase inhibitor (**ChEi**)

- Symptomatic treatments not disease-modifying
- Small but significant effect on global function and cognition
- Contraindications: bradycardia, LBBB, heart block, chronic diarrhea, weight loss/anorexia, prolonged QT
- Now fully covered on NS Pharmacare w/o exception status form



Pharmacological Therapy



- Most common side effects are GI Sx, tend to settle within days
- More severe in pts <50 kg
- Sleep disrupted, nightmares take in AM with food
- Syncope, bradycardia, QT prolongation espec w SSRIs, antipsychotics
- **Urinary incontinence**, rhinorrhea, sialorrhea, diarrhea, (all the rrheas)
- Agitation, panic-like state
- Lower seizure threshold theoretical risk not seen in practice

Starting Therapy



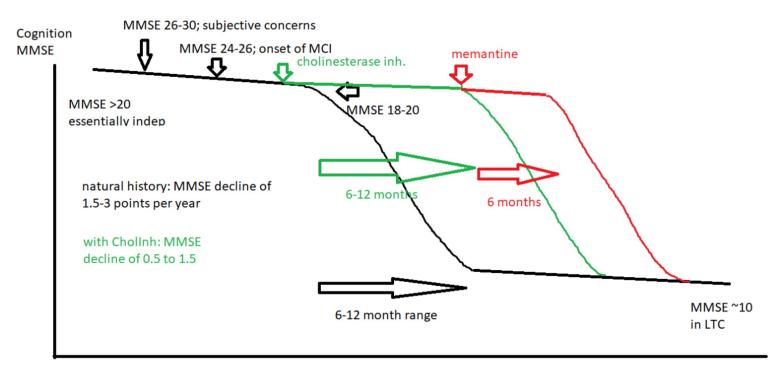
Donepezil - start 5 mg OD, increase to 10 mg after 4 weeks; +/- food; in AM

Galantamine - start 8 mg OD, increase by 8 mg q4 weeks to max 24 mg OD; with fat-containing food; in AM

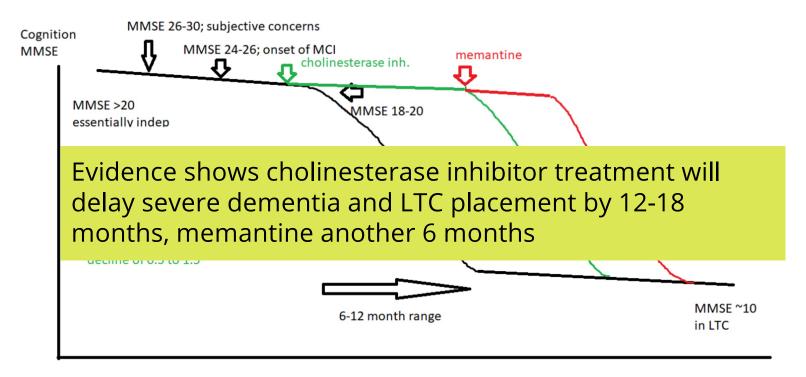
Rivastigmine - PO start 1.5 mg BID, add 1.5 mg q 4 weeks to maximum 6 mg BID; with food. TD 4.8 mg/24h, increase to 9.5 mg/24h after 4 weeks

Memantine - not covered by pharmacare, indicated for BPSD in advanced/severe dementia, minimal side effects. Now generic, \$65/month

Treatment Effects ChEis+ Memantine



Treatment Effects ChEis+ Memantine



ARTICLE

OPEN ACCESS

CLASS OF EVIDENCE

Long-term Effects of Cholinesterase Inhibitors on Cognitive Decline and Mortality

Hong Xu, MD, PhD,* Sara Garcia-Ptacek, MD, PhD,* Linus Jönsson, PhD, Anders Wimo, MD, PhD, Peter Nordström, MD, PhD, and Maria Eriksdotter, MD, PhD

Neurology® 2021;96:e2220-e2230. doi:10.1212/WNL.000000000011832

Correspondence Dr. Xu hong.xu.2@ki.se

Xu H, Garcia-Ptacek S, Jönsson L, Wimo A, Nordström P, Eriksdotter M. Long-term Effects of Cholinesterase Inhibitors on Cognitive Decline and Mortality. *Neurology*. 2021;96(17):e2220-e2230. doi:10.1212/WNL.000000000011832

Results

The matched cohort included 11,652 ChEI users and 5,826 nonusers. During an average of 5 years of follow-up, 255 cases developed severe dementia, and 6,055 (35%) died.

ChEI use was associated with higher MMSE score at each visit (0.13 MMSE points per year; 95% confidence interval [CI] 0.06–0.20). ChEI users had a 27% lower risk of death (0.73, 95% CI 0.69–0.77) compared with nonusers. Galantamine was associated with lower risk of death (0.71, 95% CI 0.65–0.76) and lower risk of severe dementia (0.69, 95% CI 0.47–1.00) and had the strongest effect on cognitive decline of all the ChEIs (0.18 MMSE points per year, 95% CI 0.07–0.28).

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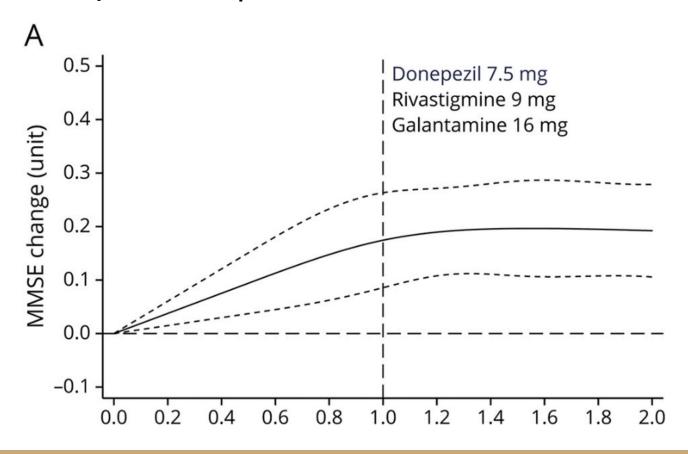
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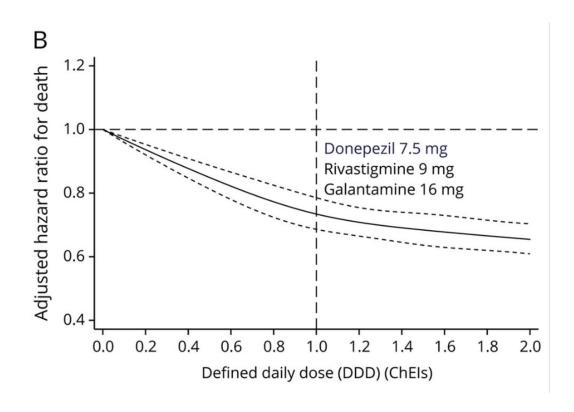
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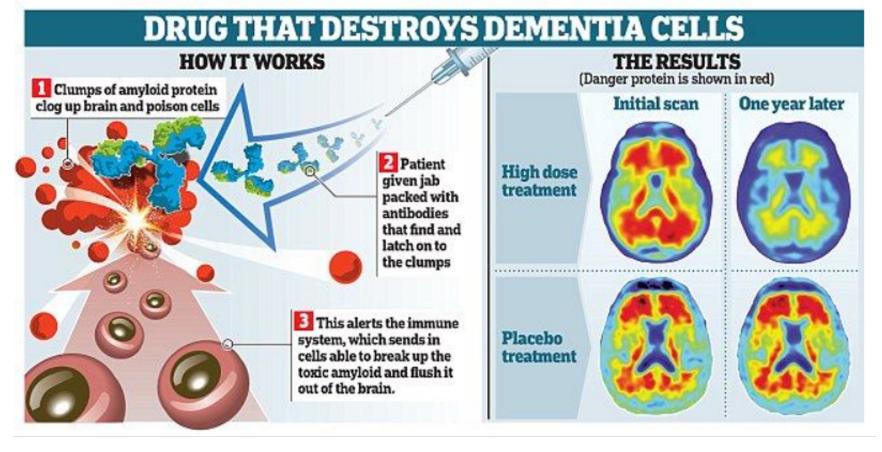
Dose Response: ↑MMSE Scores vs Non-Users



Dose Response: HR Death Compared to Population



ADUHELM/aducanumab



- Side effects intolerable, disabling: syncope or bradycardia; weight loss;
 N/V/D (may consider switch to different ChEI or manage Sx with antiemetic, anti-diarrheal; cardiology referral, may require PM for bradycardia or heart block)
- Patient non-adherence
- Decline while on treatment greater than before treatment
- Patient/family wishes





- Not necessarily when admitted to LTC
- Not based on MMSE alone but consider function
- ?Lack of effectiveness/Loss of response consider switch to another ChEI
- Donepezil has longest t½ (70h)
- Patient may decline to stage where they would have been w/o treatment + unable to regain losses once ChEI restarted

Nursing home placement in the Donepezil and Memantine in Moderate to Severe Alzheimer's Disease (DOMINO-AD) trial: secondary and post-hoc analyses



Robert Howard, Rupert McShane, James Lindesay, Craig Ritchie, Ashley Baldwin, Robert Barber, Alistair Burns, Tom Dening, David Findlay, Clive Holmes, Robert Jones, Roy Jones, Ian McKeith, Ajay Macharouthu, John O'Brien, Bart Sheehan, Edmund Juszczak, Cornelius Katona, Robert Hills, Martin Knapp, Clive Ballard, Richard G Brown, Sube Banerjee, Jessica Adams, Tony Johnson, Peter Bentham, Patrick P J Phillips

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Interpretation Withdrawal of donepezil in patients with moderate-to-severe Alzheimer's disease increased the risk of nursing home placement during 12 months of treatment, but made no difference during the following 3 years of follow-up. Decisions to stop or continue donepezil treatment should be informed by potential risks of withdrawal, even if the perceived benefits of continued treatment are not clear.

Non-Pharmacological Treatment

- Exercise is associated with improved cognition in both healthy and affected individuals - 150 min/wk of moderate intensity exercise with 2-3 days of resistance training
- Mediterranean diet, MIND diet
- Sleep optimization
- Minimize EtOH
- Social engagement we saw the results of a natural experiment during COVID-19 lockdowns
- No evidence for nutritional supplements, sudoku, crossword puzzles

ORIGINAL ARTICLE

Trial of the MIND Diet for Prevention of Cognitive Decline in Older Persons

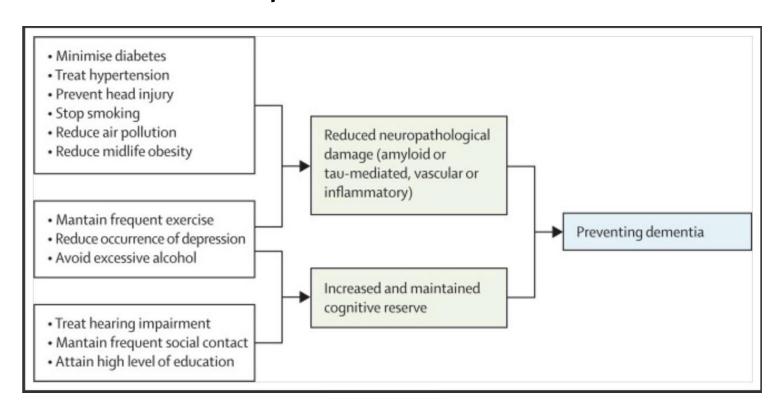
L.L. Barnes, K. Dhana, X. Liu, V.J. Carey, J. Ventrelle, K. Johnson, C.S. Hollings, L. Bishop, N. Laranjo, B.J. Stubbs, X. Reilly, P. Agarwal, S. Zhang, F. Grodstein, C.C. Tangney, T.M. Holland, N.T. Aggarwal, K. Arfanakis, M.C. Morris,* and F.M. Sacks

CONCLUSIONS

Among cognitively unimpaired participants with a family history of dementia, changes in cognition and brain MRI outcomes from baseline to year 3 did not differ significantly between those who followed the MIND diet and those who followed the control diet with mild caloric restriction. (Funded by the National Institute on

Aging; ClinicalTrials.gov number, NCT02817074.)

Take Home Points from Lancet Commission 2020



Rush Memory and Aging Project

THE LANCET Neurology

Investigation of frailty as a moderator of the relationship between neuropathology and dementia in Alzheimer's disease: a cross-sectional analysis of data from the Rush Memory and Aging Project

Lindsay M K Wallace, MSc • Olga Theou, PhD • Judith Godin, PhD • Melissa K Andrew, MD • Prof David A Bennett, MD • Prof Kenneth Rockwood, MD &
Published: February, 2019 • DOI: https://doi.org/10.1016/S1474-4422(18)30371-5 • Check for updates

Rush Memory and Aging Project

Some people with substantial Alzheimer's disease pathology at autopsy had shown few characteristic clinical symptoms or signs of the disease, whereas others with little Alzheimer's disease pathology have been diagnosed with Alzheimer's dementia.

We aimed to examine whether frailty ... moderates the relationship between Alzheimer's disease pathology and Alzheimer's dementia.

The degree of frailty among people of the same age modifies the association between Alzheimer's disease pathology and Alzheimer's dementia.

Rockwood Clinical Frailty Scale

CLINICAL FRAILTY SCALE

ţ	1	VERY FIT	People who are robust, active, energetic and motivated. They tend to exercise regularly and are among the fittest for their age.
•	2	FIT	People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g., seasonally.
t	3	MANAGING Well	People whose medical problems are well controlled, even if occasionally symptomatic, but often are not regularly active beyond routine walking.
•	4	LIVING WITH VERY MILD FRAILTY	Previously "vulnerable," this category marks early transition from complete independence. While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up" and/or being tired during the day.
A	5	LIVING WITH MILD FRAILTY	People who often have more evident slowing, and need help with high order instrumental activities of daily living (finances, transportation, heavy housework). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation, medications and begins to restrict light housework.



SCORING FRAILTY IN PEOPLE WITH DEMENTIA

The degree of fruity generally corresponds to the degree of dementia. Common symptoms in mild dementia include longetting the details of a recent event, though still remembering the event itself, respecting the same question/story and social withdrawal.

In moderate dementia, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting. In severe dementia, they cannot do

personal care without help. In very severe dementia they are often bedfast. Many are virtually mute.



Clinical Frailty Scale 0/2006–2020 Rockwood, Version 2.0 (DN), All rights reserved. For permission: www.geristricemedicinversearch, ca Rockwood Ket al. A global clinical measure of fitness and frailty in eldenly people. ONAJ 2005;172-489–495.

Lancet 2020 Commission - Dementia

The Lancet Commissions

Dementia prevention, intervention, and care: 2020 report of @ 🦒 📵 the Lancet Commission



Gill Livingston, Jonathan Huntley, Andrew Sommerlad, David Ames, Clive Ballard, Sube Banerjee, Carol Brayne, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Sergi G Costafreda, Amit Dias, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Mika Kivimäki, Eric B Larson, Adesola Oqunniyi, Vasiliki Orgeta, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk, Linda Teri, Naaheed Mukadam

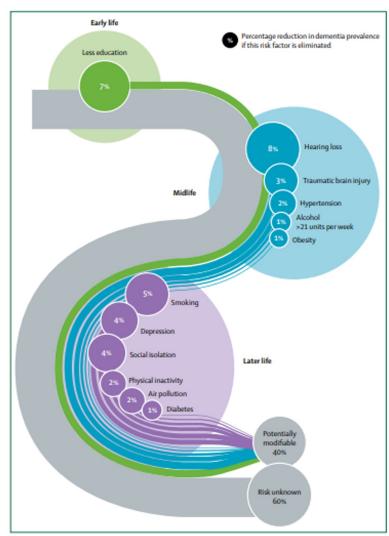


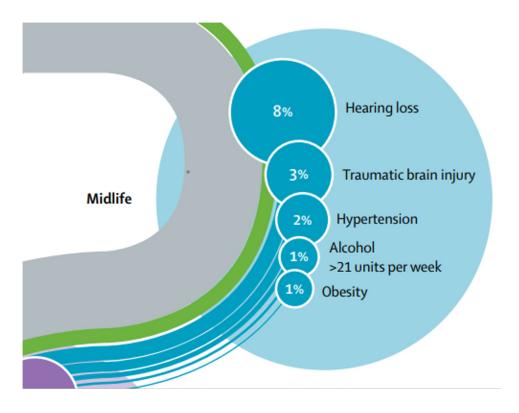
Figure 7: Population attributable fraction of potentially modifiable risk factors for dementia



Early Life

Genetic: ApoE $\epsilon 4 = 7\%$

Low Education - 7%



Midlife

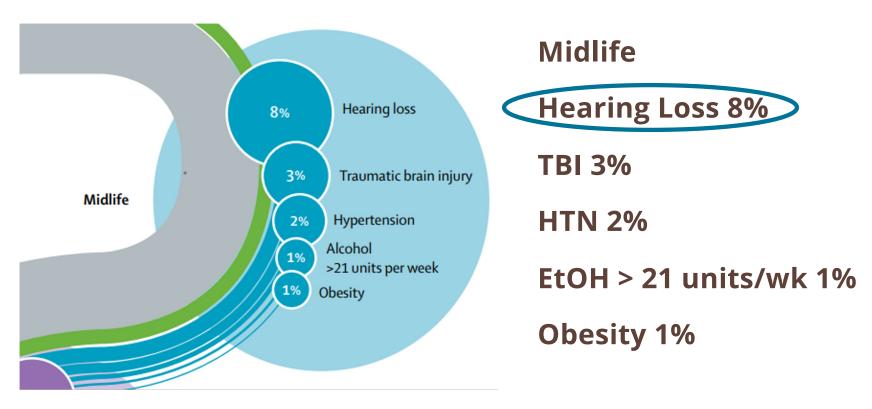
Hearing Loss 8%

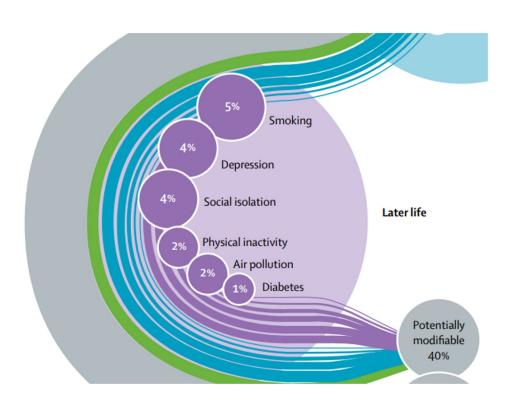
TBI 3%

HTN 2%

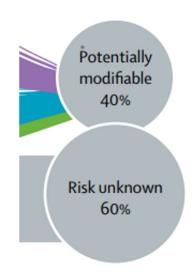
EtOH > 21 units/wk 1%

Obesity 1%





Later Life
Smoking 5%
Depression 4%
Social Isolation 4%
Physical Inactivity 2%
Air Pollution 2%
Diabetes 1%



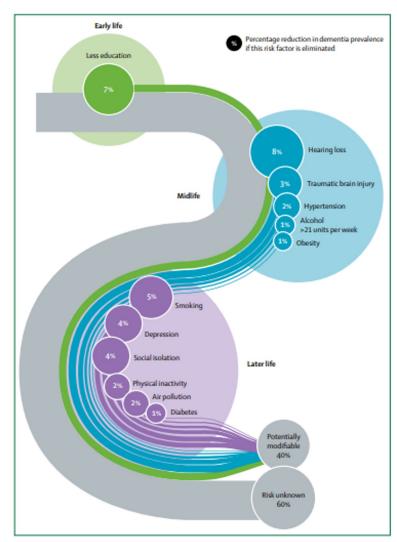


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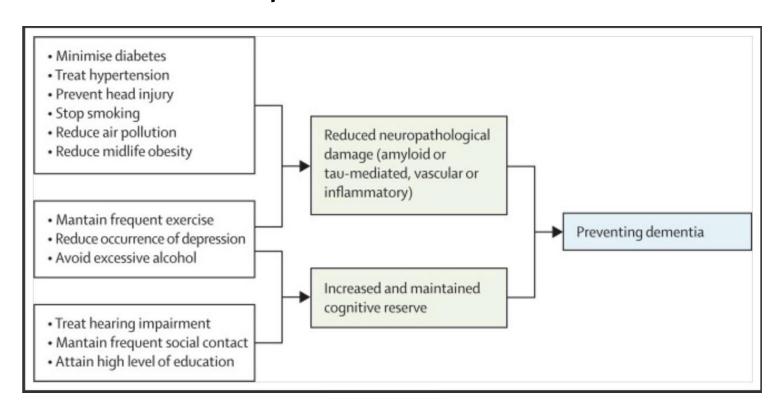
Relative Risk

Risk Factor	AD	VaD
DM	1.46	2.28
Midlife HTN	1.61	1.59
Midlife Obesity	1.60	1.33
Physical Inactivity	1.82	1.61
Depression	1.65	2.92
Smoking	1.59	1.26
Low Education	1.59	2.75

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DM	1.46	2.28
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Physical Inactivity	1.82	1.61
Depression	1.65	2.92
Smoking	1.59	1.26
Low Education	1.59	2.75

Take Home Points from Lancet Commission 2020

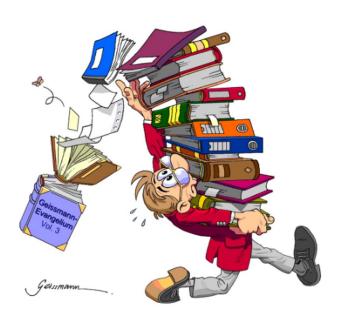


Take Home Points

Dementia prevalence is increasing
Incidence is declining in high income countries
It is a big part of primary care
FPs have been managing dementia patients
successfully for many years
Be aware of Beer's Criteria, effect of Rx on
cognition - benzos, pain meds, EtOH



Take Home Points



Must assess function to diagnose dementia

Start AChEIs at diagnosis and monitor for improvements and side effects

Consider most prominent symptom/impairment for Dx

Phone a friend if you are not sure.

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