
Deprescribing for Brain Health

From individualized care to large scale interventions

Camille Gagnon, PharmD

Assistant Director, Canadian Deprescribing Network



CaDeN
Canadian Deprescribing
Network



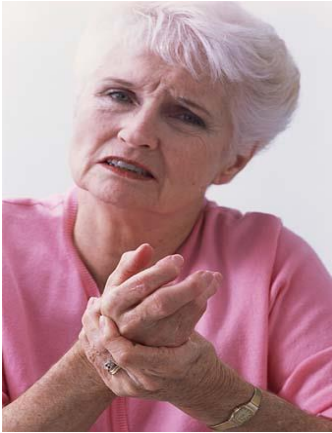
Objectives

1. Review the facts of polypharmacy and the associated risks
2. Describe how specific medications affect memory and cognition
3. Develop a systematic approach to the implementation of deprescribing practices to help preserve brain health

No conflict of interest to declare

Mrs. S. is worried because she can't find her car in the parking lot

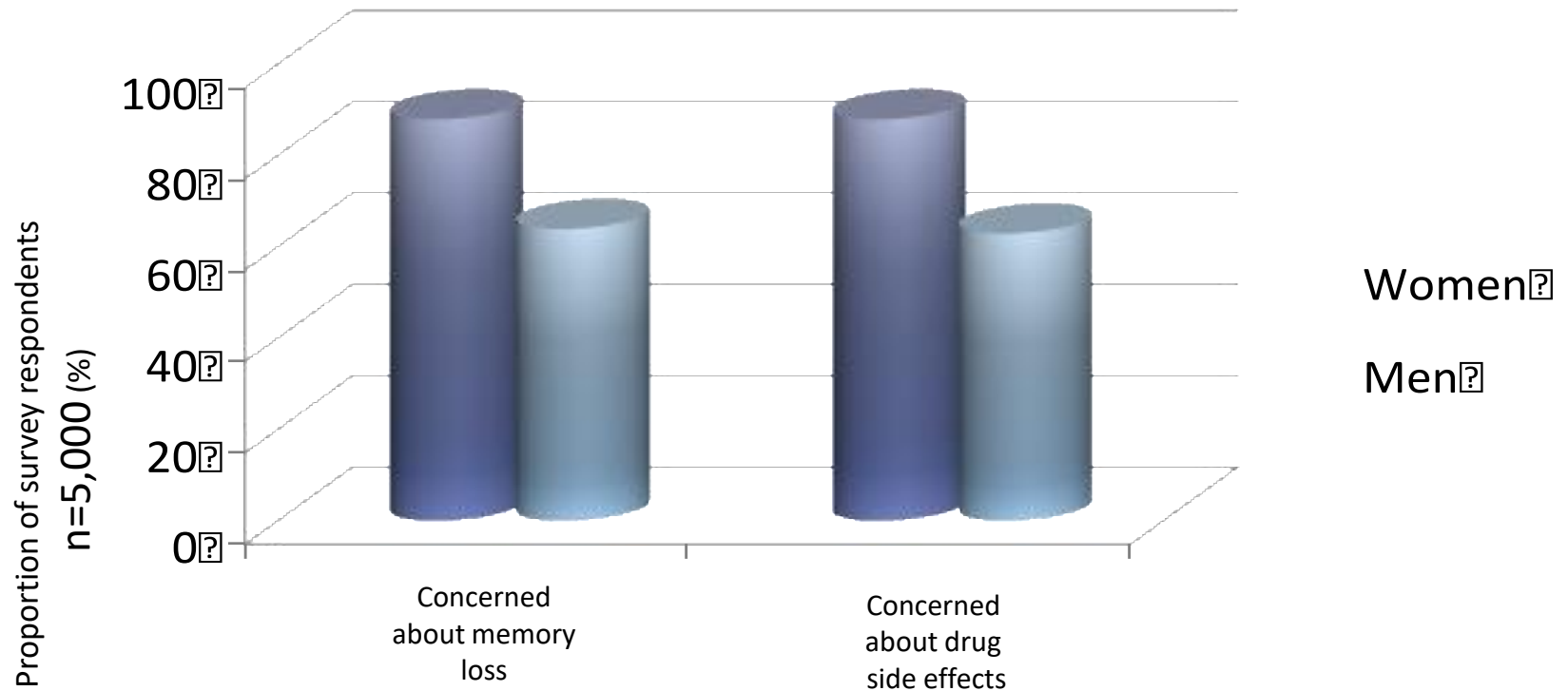
Her medications include



72 years old

- Sleeping pill (Ativan®)
- A pill for her vertigo (Gravol®)
- A pill for muscle spasm (Flexeril®)
- An antidepressant (Elavil®)

Top ranked health concerns among aging men & women in Canada



Tannenbaum et al. CMAJ 2005
Tannenbaum. Aging Male 2012

CaDeN
Canadian Deprescribing
Network



ReCaD
Réseau canadien
pour la déprescription

The facts: In Canada, what proportion of community dwelling seniors takes...



5 or more meds?

Canadian Institute for Health Information. Drug Use Among Seniors on Public Drug Programs in Canada, May 2014.

The facts: In Canada, what proportion of community dwelling seniors takes...



5 or more meds?

66%

Canadian Institute for Health Information. Drug Use Among Seniors on Public Drug Programs in Canada, May 2014.

The facts: In Canada, what proportion of community dwelling seniors takes...



5 or more meds?

66%



10 or more meds?

Canadian Institute for Health Information. Drug Use Among Seniors on Public Drug Programs in Canada, May 2014.

The facts: In Canada, what proportion of community dwelling seniors takes...



5 or more meds?

66%



10 or more meds?

27%

Canadian Institute for Health Information. Drug Use Among Seniors on Public Drug Programs in Canada, May 2014.

The facts: In Canada, what proportion of community dwelling seniors takes...



5 or more meds?

66%



10 or more meds?

27%

What proportion of 85+ year olds take 10+ meds?

Canadian Institute for Health Information. Drug Use Among Seniors on Public Drug Programs in Canada, May 2014.

The facts: In Canada, what proportion of community dwelling seniors takes...



5 or more meds?

66%



10 or more meds?

27%

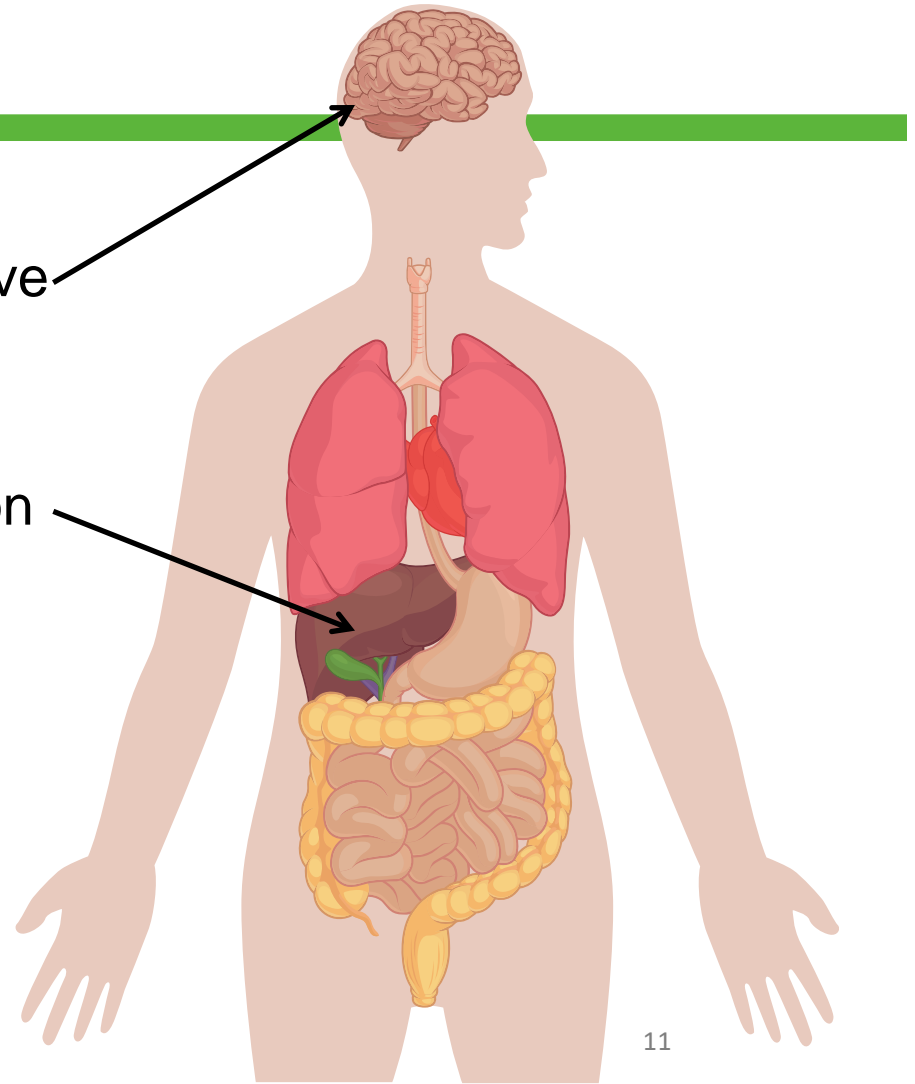
What proportion of 85+ year olds take 10+ meds?

39%

Canadian Institute for Health Information. Drug Use Among Seniors on Public Drug Programs in Canada, May 2014.

As we age

- Blood-brain barrier not as effective
- Higher fat content in body – fat soluble drugs accumulate
- Reduced kidney and liver function
- Reduced water (fluid) in body – water-soluble drugs more concentrated



11

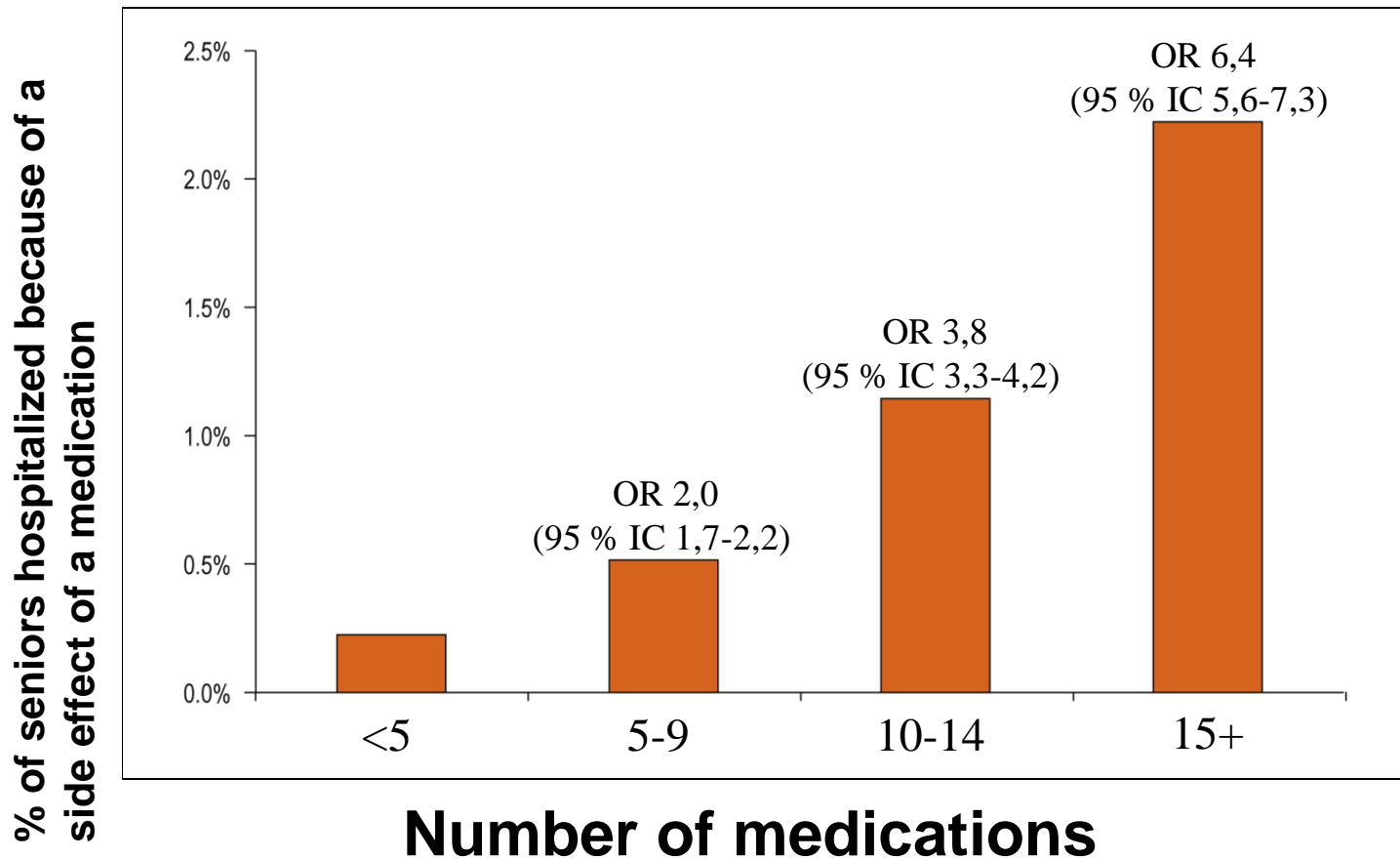
Problems with polypharmacy

1. Side effects
2. Interactions
3. Hospitalisations
4. Costs

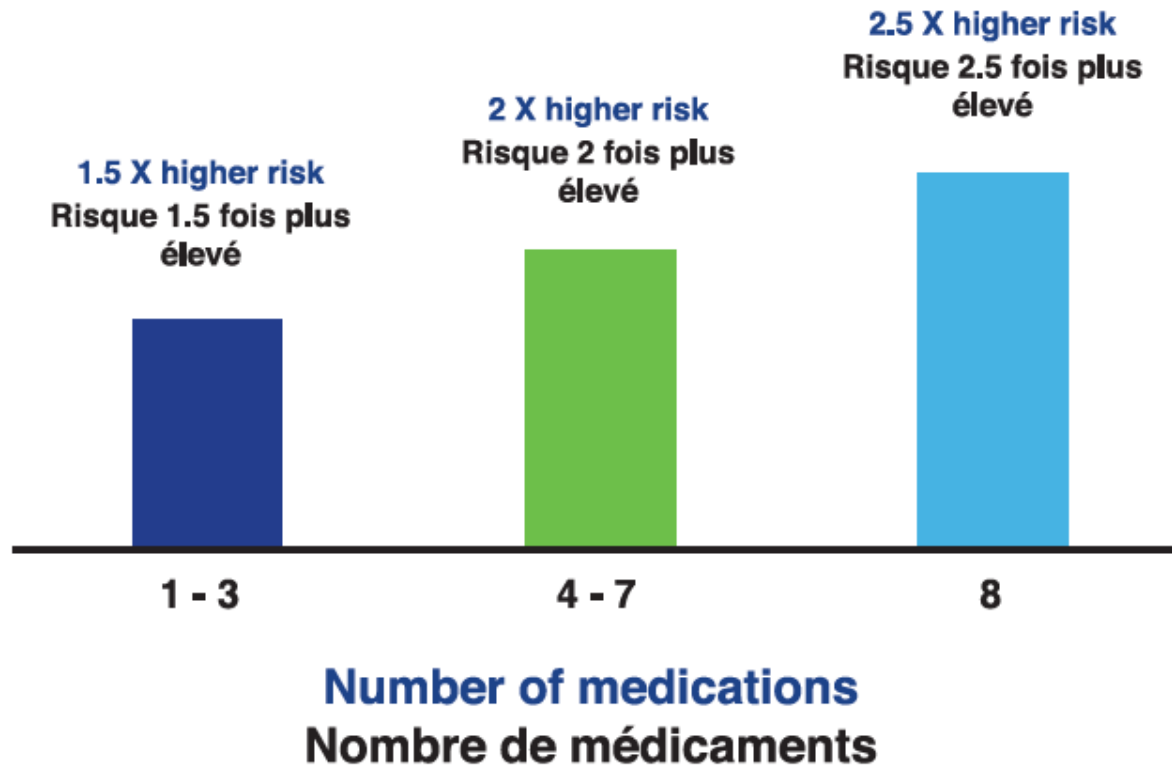


More medications
leads to more...

Polypharmacy increases the risk of hospitalizations linked to medication



Risk of falling increases with number of medications



Adapted from / Adapté de Zierns et al. 2006

Polypharmacy often comes with...

- Prescribing cascade
- Poor adherence to treatment
- Errors/confusion in managing medication



Who is most at risk of harmful effects of medication?

1. People with multiple chronic conditions
2. Women
3. People over the age of 65



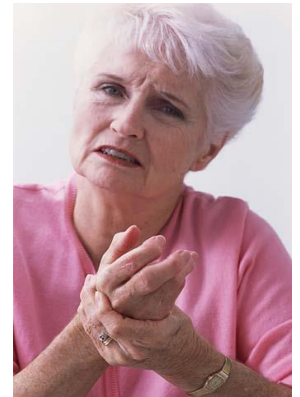
Each year in Canada:

- **1 in 143 seniors are hospitalized** due to harmful effects of their medication.

Women are more at risk

In 2014, the FDA and Health Canada recommended to cut the dose of zolpidem (Sublinox) in half for women

- Women metabolize zolpidem differently with blood concentrations 45% higher than in men
- Women are at greater risk of not eliminating the medication the next day, which puts them at risk of impaired driving



Women are more at risk



Women are more at risk. Why?

- Longer life expectancy
- Suffer from more chronic conditions
- Take more medication
- Female biology and physiology increases the risk of harmful effects of medication

The cost of potentially inappropriate medication

\$419 million

Canadians spend \$419M per year on potentially harmful prescription medications. This does not include hospital costs.

\$1.4 billion

Canadians spend \$1.4B per year in health care costs to treat harmful effects from medications, including fainting, falls, fractures and hospitalizations.

Morgan *et al.* 2016. CMAJ Open; 4: E346-E51.

Inappropriate Prescriptions

Risk > Benefit, alternative therapies exist

AGS BEERS

CRITERIA 2012

AGS Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults (2015)

Benzodiazepines

Temazepam
Oxazepam
Lorazepam
Alprazolam
Clonazepam
Diazepam
Flurazepam
Clorazepate

All antipsychotics

Non-benzodiazepine sedative hypnotics

Zolpidem
Zopiclone
Zaleplon

Sulfonylurea oral hypoglycemics

Glyburide
Glipizide
Chlorpropamide

Tricyclic antidepressants

Amitriptyline
Imipramine

1st generation antihistamines

Hydroxyzine
Diphenhydramine

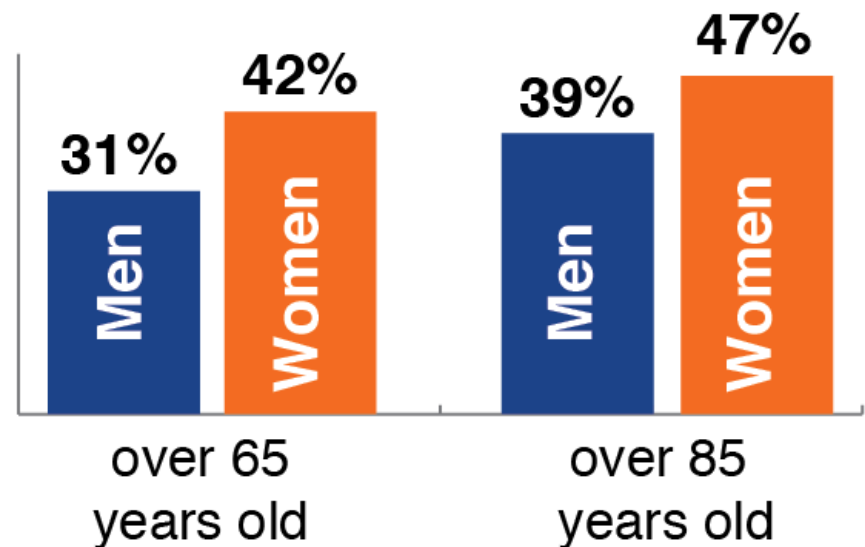
Cardiovascular/diuretic agents

Amiodarone
Digoxin > 0.125 mg/day

Potentially inappropriate medications in Canadian seniors

Medications that pose greater health risks when prescribed for older adults, compared with available drug and non-drug alternatives.

Canadian seniors who take at least one potentially inappropriate medication



What is 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.

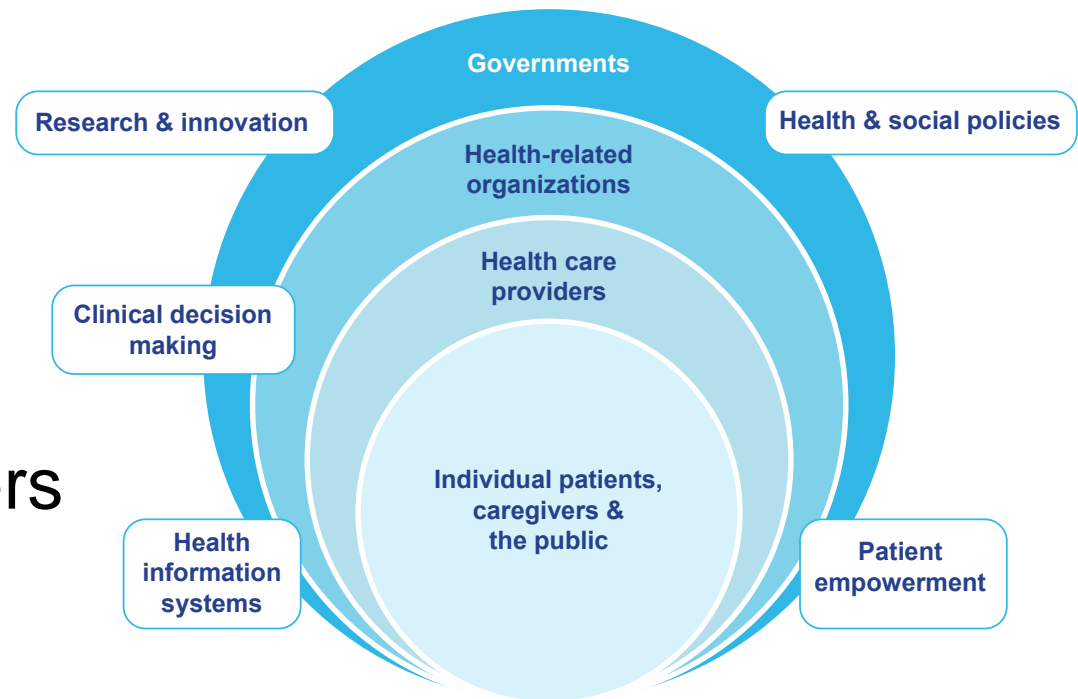
Deprescribing involves patients, caregivers, healthcare providers and policy makers.



The Canadian Deprescribing Network

The Canadian Deprescribing Network is a group of :

- Health care leaders
- Clinicians
- Decision-makers
- Academic researchers
- Patient advocates



Impact of medication on cognition: when and why deprescribe



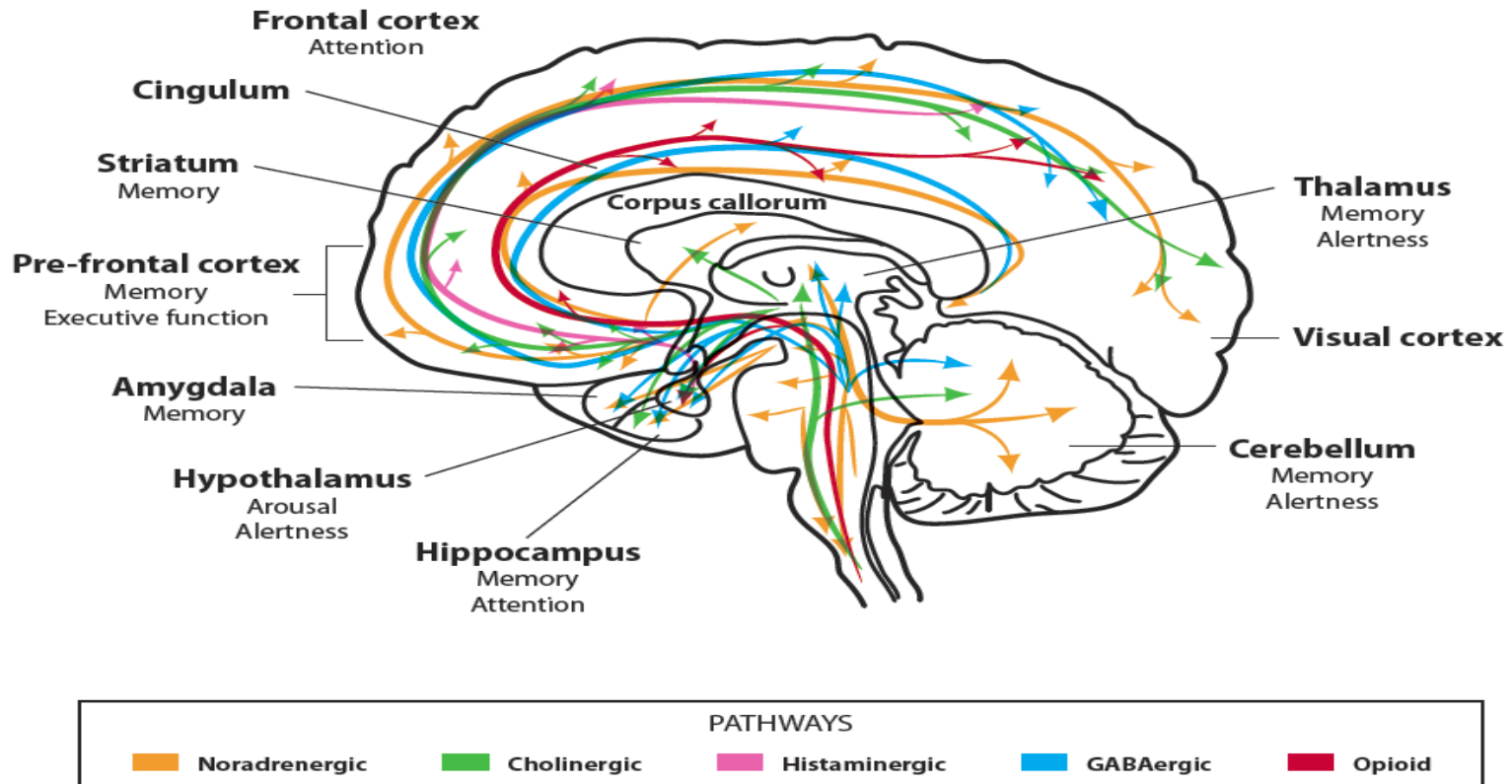
Fourth Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (2014)

*“Diagnostic criteria for **possible** AD - A diagnosis of possible AD should be made when the criteria for AD are met (regarding the nature of cognitive deficits) but the disease follows an atypical course (eg, there is a sudden onset of cognitive impairment and cognitive decline is not gradual), or when criteria for AD are met but there is evidence of a mixed presentation, such as concomitant cerebrovascular disease, or the patient has clinical features of dementia with Lewy bodies, has another comorbidity (medical or neurologic), **or is using medication that could have a substantial effect on cognition.**”*

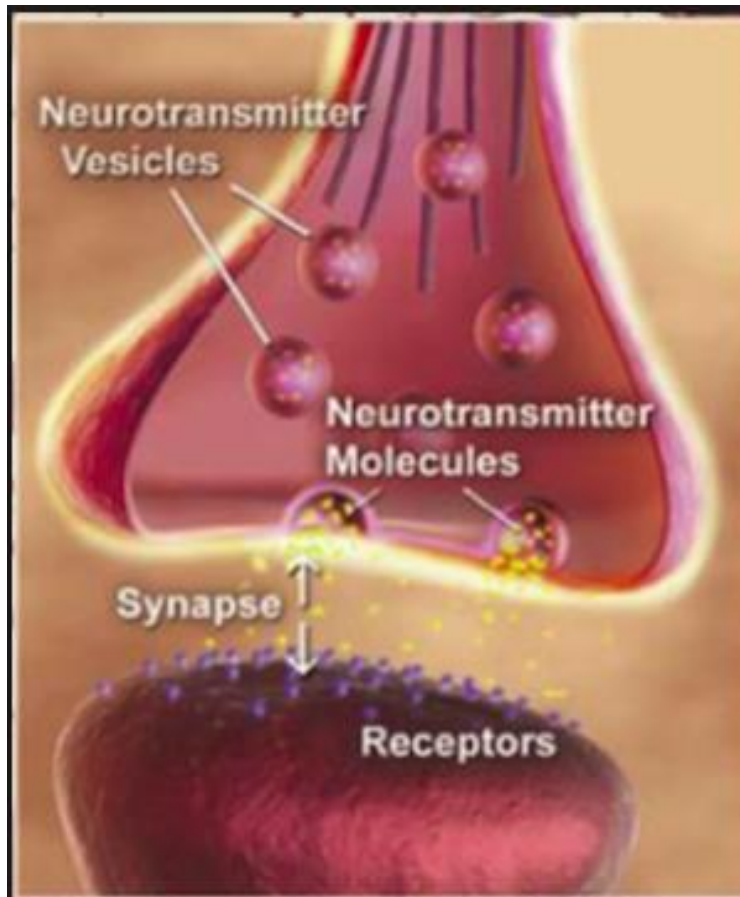
Different ways medication can negatively impact cognition

1. Anticholinergic effects
2. Sedation
3. Deficiency in vitamin B₁₂
e.g. : metformin, PPIs...
4. Hypoglycemia
5. Hypotension
6. Increasing risk of stroke

Neurotransmitter pathways involved in memory, attention, response time, executive function



Anticholinergic effects



Some anticholinergic effects:

- Agitation
- Blurred vision
- Constipation
- Dry mouth
- Sedation
- Trouble urinating
- Confusion
- Delirium

Examples of highly anticholinergic drugs

Drug class	Commercial/Generic names
Antihistamines	Benadryl (diphenhydramine); Gravol (dimenhydrinate); Chlor-Tripolon (chlorpheniramine); Atarax (hydroxyzine)
Tricyclic antidepressants	Elavil (amitriptyline); Aventyl (nortriptyline); imipramine; desipramine
Antimuscarinics	Ditropan (oxybutynin); Detrol (tolterodine); Enablex (darifenacin); Vesicare (solifenacin); Toviaz (fesoterodine)
Antipsychotics	Clozaril (clozapine); Haldol (haloperidol); Zyprexa (olanzapine); Seroquel (quetiapine)
Muscle relaxants	Robaxin (methocarbamol); Orfenace (orphenadrine); Lioresal (baclofen); Flexeril (cyclobenzapine)
Antiparkinsonians	Cogentin (benztropine)

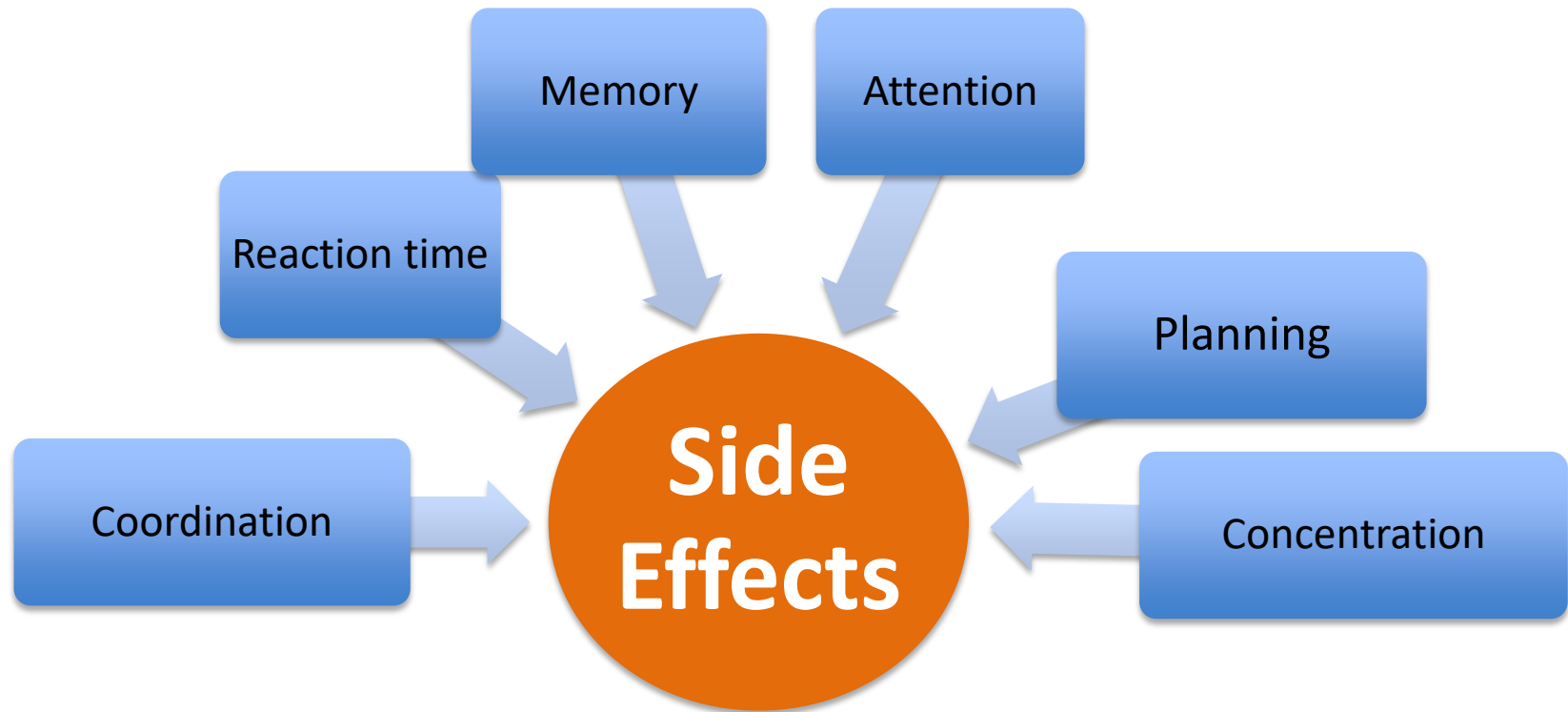
Anticholinergic burden

- Drug Burden Index (DBI)
 - Takes into account anticholinergic and sedative effects, total number of medications, daily dose
 - Associated with impaired performance in mobility and cognitive testing
- Dementia patients seeing multiple physicians leads to a higher anticholinergic burden score

Hilmer, SN et al. A drug burden index to define the functional burden of medications in older people. *Arch Intern Med.* 2007;167(8):781.

Reppas-Rindlisbacher, CE. Anticholinergic Drug Burden in Persons with Dementia Taking a Cholinesterase Inhibitor: The Effect of Multiple Physicians. *J Am Geriatr Soc.* 2016 Mar; 64(3): 492–500.

Sleeping pills affect many cognitive processes



Drug-induced amnestic vs. non-amnestic cognitive dysfunction

Drug class	Amnestic deficits: short or long-term memory	Non-amnestic deficits: concentration/information processing/planning/ psychomotor speed
Benzodiazepines	✓ ✓ ✓	✓ ✓ ✓
Non-benzodiazepines	✓	✓
1 st generation antihistamines	✓	✓ ✓ ✓
Tricyclic antidepressants	✓	✓ ✓ ✓
Other anticholinergics	✓	✓
Opioid drugs	✓	✓

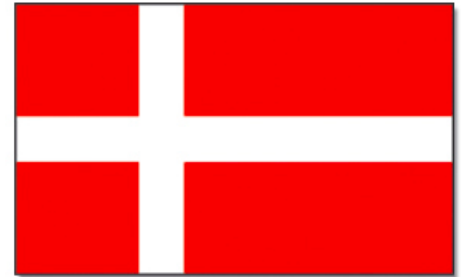
Tannenbaum, Paquette, Hilmer, Holroyd-Leduc, Carnahan. A systematic review of amnestic and non-amnestic mild cognitive impairment induced by antihistamine, anticholinergic, GABAergic and opioid drugs. *Drugs Aging* 2012;29: 639-658

Harms of benzodiazepines on cognition

- Induces amnestic and non-amnestic cognitive impairment
 - Evidence of dose-response relationship
- Motor vehicle accidents
 - Comparable to driving above the alcohol limit
- Daytime fatigue
- Dementia?

Denmark is not taking any chances...

- **Denmark's** Driver Licensing Incentive Policy
- Seniors on strong sleeping pills not allowed to renew their driving license
- Seniors on moderate sleeping pills get a 1-year conditional renewal, cognitive testing every year
- New users not allowed to drive for 4 weeks
- Episodic users recommended not to drive the next day



Effectiveness of CBTi versus sedative-hypnotics

CBTi

- **Sleep onset latency**
 - Post-treatment **-23 minutes** (-37 to -10)
 - 12 months -17 (-30 to -4)
- **Total wake time at night**
 - Post **-68 minutes** (-96 to -40)
 - 12 months -31 (-58 to -4)
- **Sleep efficiency**
 - Post +10% (5% to 15%)
 - 12 months +5% (0.5% to 10%)

Alessi et al. J Am Geriatr Soc 2016

Benzos & Z-drugs

- **Sleep onset latency**
 - **-22 minutes** (95% CI 11-33 minutes), compared to placebo
- **NNT** to improve sleep quality = 13
- **Total wake time at night**
 - Post **-25 minutes** (-38 to -13) vs placebo
- **Decrease in total number of awakenings**
 - 0.63 (- 0.48 to - 0.77) vs placebo

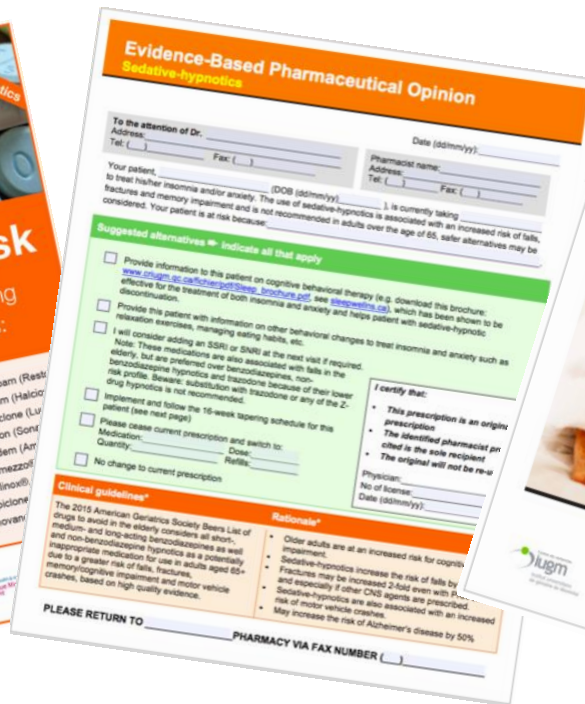
Glass et al. Meta-analysis. BMJ 2005
Huedo-Medina et al. Meta-analysis 2012

Start deprescribing!



Engage patients and other health providers

- Use evidence-based tools



The EMPOWER trial

- ✓ Test whether a **direct-to-consumer educational brochure** is effective at reducing benzos, compared to usual care
- ✓ Cluster randomized trial where:
 - ✓ The cluster is the community pharmacy from whence patients are recruited
 - ✓ Randomization is whether the patient gets the **mailed brochure** immediately or after a 6-month waiting period
 - ✓ Inclusion criteria = benzo use for 3 months+, aged 65+
- ✓ Post-hoc analysis also done on the effects of the EMPOWER brochure in patients with mild cognitive impairment

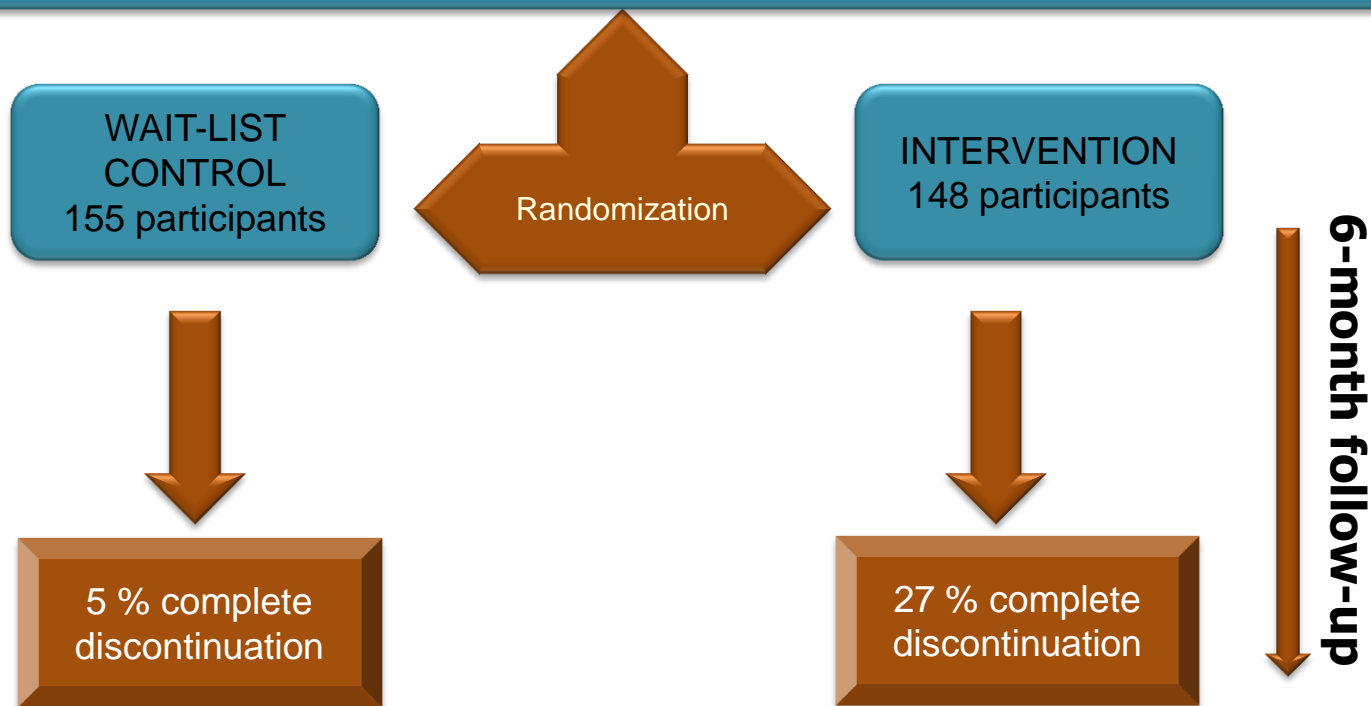
Martin P et al. An educational intervention to reduce the use of potentially inappropriate medications among older adults (EMPOWER study): protocol for a cluster randomized trial. Trials. 2013 Mar 20;14:80.

EMPOWER trial hypothesis

If patients were aware of the risks associated with benzodiazepine use, then they would opt to discontinue...

EMPOWER = “Eliminating medications through patient ownership of end results”

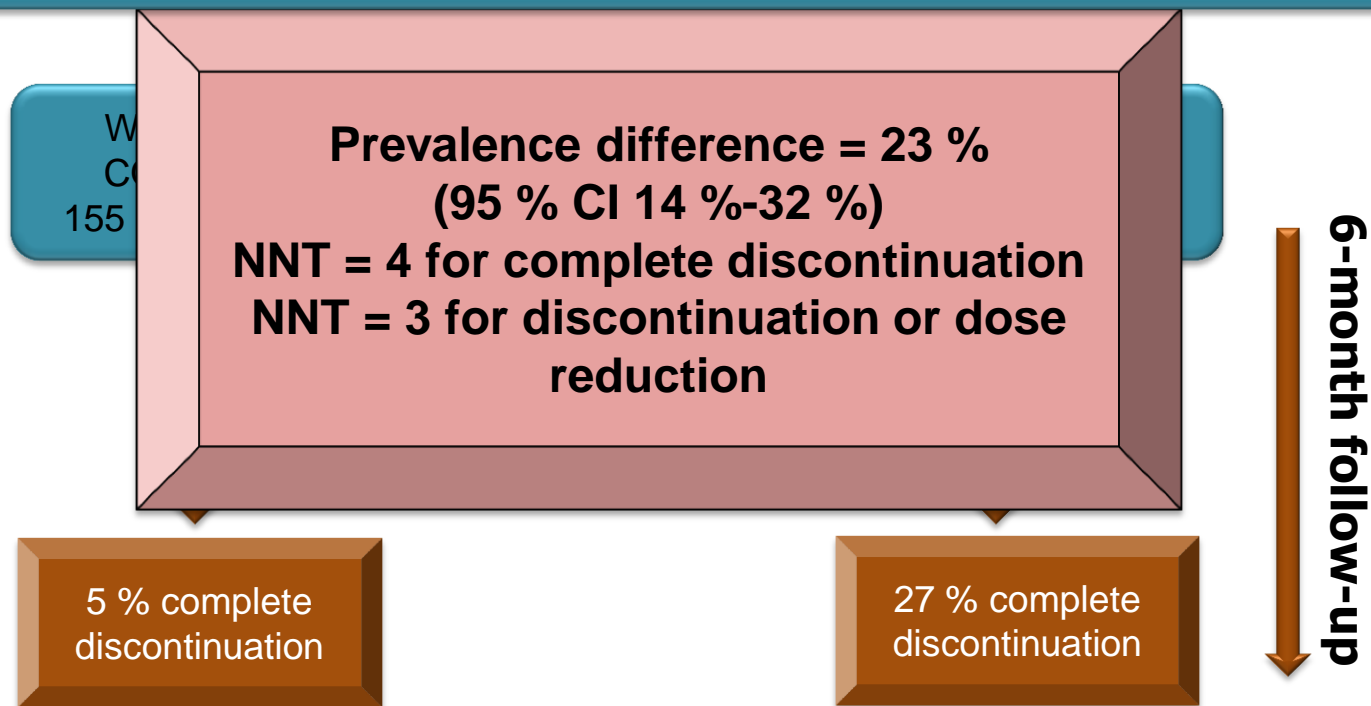
30 community pharmacies around Montreal 2,716 chronic benzo users 65+,
303 participants, benzo users 3 months+, aged 65 years and older
no dementia, not on antipsychotics
query baseline knowledge and beliefs at baseline



Tannenbaum, Martin, Tamblyn, Benedetti, Ahmed. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial. JAMA Intern Med. 2014 Jun;174(6):890-8.

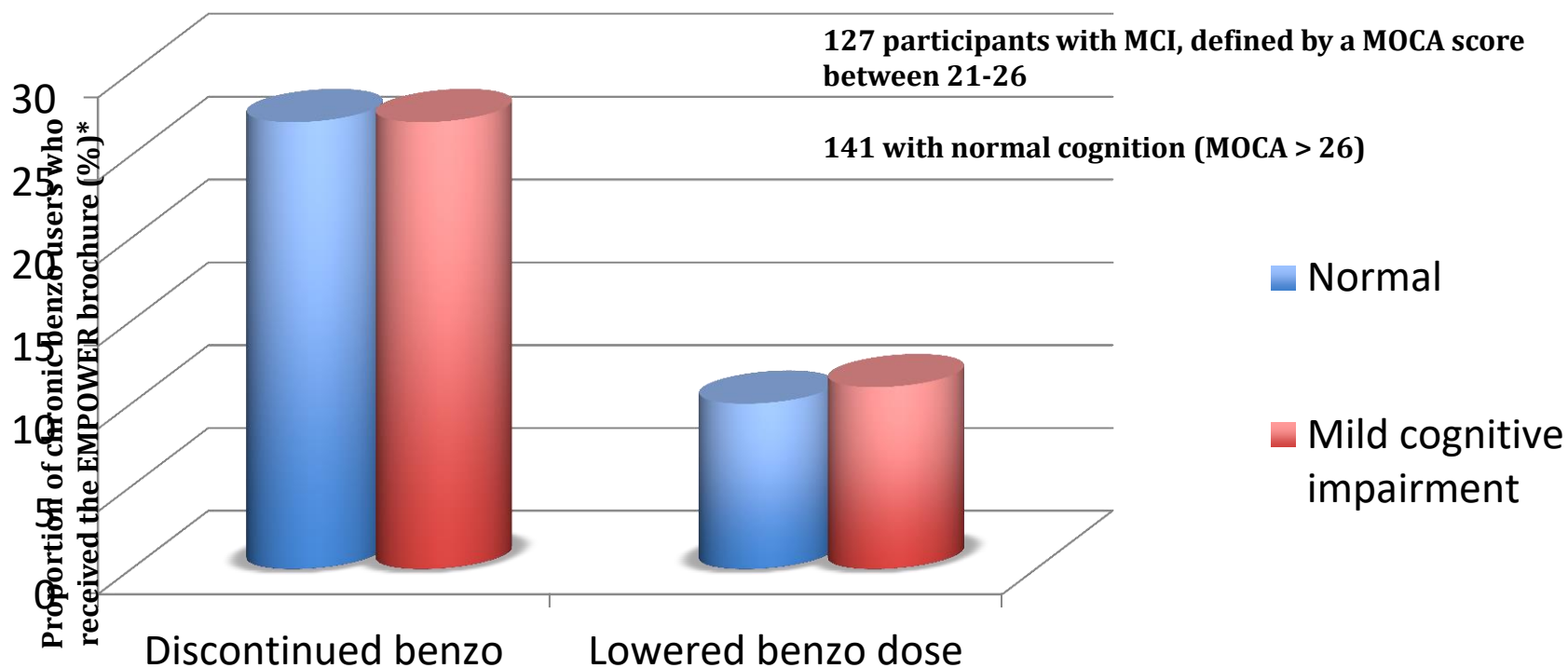
EMPOWER = “Eliminating medications through patient ownership of end results”

30 community pharmacies around Montreal 2,716 chronic benzo users 65+,
303 participants, benzo users 3 months+, aged 65 years and older
no dementia, not on antipsychotics
query baseline knowledge and beliefs at baseline



Tannenbaum, Martin, Tamblyn, Benedetti, Ahmed. Reduction of inappropriate benzodiazepine prescriptions among older adults through direct patient education: the EMPOWER cluster randomized trial. JAMA Intern Med. 2014 Jun;174(6):890-8.

EMPOWER brochure worked for persons with mild cognitive impairment (MCI)



6 month outcomes

Martin & Tannenbaum. BMC Geriatrics 2017



You May Be at Risk

You are taking one of the following sedative-hypnotic medications:

- | | | |
|---|---|---|
| <input type="radio"/> Alprazolam (Xanax®) | <input type="radio"/> Diazepam (Valium®) | <input type="radio"/> Temazepam (Restoril®) |
| <input type="radio"/> Bromazepam (Lectopam®) | <input type="radio"/> Estazolam | <input type="radio"/> Triazolam (Halcion®) |
| <input type="radio"/> Chlorazepate | <input type="radio"/> Flurazepam | <input type="radio"/> Eszopiclone (Lunesta®) |
| <input type="radio"/> Chlordiazepoxide-amitriptyline | <input type="radio"/> Loprazolam | <input type="radio"/> Zaleplon (Sonata®) |
| <input type="radio"/> Clidinium-chlordiazepoxide | <input type="radio"/> Lorazepam (Ativan®) | <input type="radio"/> Zolpidem (Ambien®, Intermezzo®, Edluar®, Sublinox®, Zolpimist®) |
| <input type="radio"/> Clonazepam (Rivotril®, Klonopin®) | <input type="radio"/> Lormetazepam | <input type="radio"/> Zopiclone (Imovane®, Rhovane®) |
| | <input type="radio"/> Nitrazepam | |
| | <input type="radio"/> Oxazepam (Serax®) | |
| | <input type="radio"/> Quazepam | |

You May Be at Risk

You are currently taking a sulfonylurea diabetic medication:

- Chlorpropamide (Diabinese®, Glucamide®)
- Glyburide (DiaBeta®, Glynase® PresTab®, Micronase®)

TEST YOUR KNOWLEDGE ABOUT THIS MEDICATION



QUIZ

SEDATIVE-HYPNOTIC DRUGS

1. The medication I am taking is a mild tranquilizer that is safe when taken for long periods of time. TRUE FALSE
2. The dose I am taking causes no side effects. TRUE FALSE
3. Without this medication I will be unable to sleep or will experience unwanted anxiety. TRUE FALSE
4. This medication is the best available option to treat my symptoms. TRUE FALSE



ANSWERS



1. FALSE

It is no longer recommended to take a sedative-hypnotic drug to treat insomnia or anxiety. People who these medications are putting themselves at an increased risk of side effects:

- 5-fold higher risk of memory and concentration problems
- 4-fold increased risk of daytime fatigue
- 2-fold increased risk of falls and fractures (hip, wrist)
- 2-fold increased risk of having a motor vehicle accident

2. FALSE

Even if you think that you have no side effects, and even if you take only a small dose, a sedative-hypnotic drug worsens your brain performance and slows your reflexes.

3. TRUE

Your body has probably developed a physical addiction to this medication. If you stop it abruptly, you may have trouble sleeping and feel greater anxiety. Millions of people have succeeded in slowly cutting this drug out of their lives and/or have found alternative treatments.

4. FALSE

Although it is effective over the short term, studies show that sedative-hypnotic drugs are not the best long-term treatment for anxiety or insomnia. Sedative-hypnotic medication covers up the symptoms without actually solving the problem. Please keep on reading to learn more about developing healthier sleep patterns and diminishing stress.

ALTERNATIVES

Are you taking this sedative-hypnotic drug to help reduce your anxiety?

There are other solutions to deal with your stress and anxiety:

- Talking to a therapist is a good way to get help to work through stressful situations and identify the sources of your anxiety.
- Support groups can help relieve your stress and make you feel you are not alone.
- Relaxation techniques like stretching, yoga, massage, meditation or tai chi can help relieve your everyday stress and aid you in working through anxiety.
- Talk to your doctor about other anti-anxiety medications that have less serious side effects.



MRS. ROBINSON'S STORY

She had been taking lorazepam, a sedative-hypnotic drug just like yours

"I am 65 years old and took lorazepam for 10 years. A few months ago, I fell in the middle of the night on my way to the bathroom and had to go to the hospital. I was lucky and, except for some bruises, I did not hurt myself. I read that lorazepam puts me at risk for falls. I did not know if I could live without lorazepam as I always have trouble falling asleep and sometimes wake up in the middle of the night.
































































I spoke to my doctor who told me that my body needs less sleep at my age – 6 hours of sleep per night is enough. That's when I decided to try to taper off lorazepam. I spoke to my pharmacist who suggested I follow the step-by-step tapering program (on the next page).

I also applied some new sleeping habits I had discussed with my doctor. First, I stopped exercising before bed; then, I stopped reading in bed; and finally, I got out of bed every morning at the same time whether or not I had a good night's sleep.

I succeeded in getting off lorazepam. I realize now that for the past 10 years I have not been living to my full potential. Stopping lorazepam has lifted a veil – it's like I had been semi-sleeping my life away. I have more energy and don't have so many ups and downs anymore. I am more alert: I don't always sleep well at night, but I don't feel as groggy in the morning. It was my decision! I am so proud of what I have accomplished. If I can do it, so can you!"

TAPERING-OFF PROGRAM

We recommend that you follow this schedule under the supervision of your doctor, nurse or pharmacist.

WEEKS	TAPERING SCHEDULE							✓
	MO	TU	WE	TH	FR	SA	SU	
1 and 2								
3 and 4								
5 and 6								
7 and 8								
9 and 10								
11 and 12								
13 and 14								
15 and 16								
17 and 18								

EXPLANATIONS

 Full dose  Half dose  Quarter of a dose  No dose

Great CBTi Resources



Insomnia Sleeping Pills CBTi

Sleepwell

**It's no dream.
Sleep well without sleeping pills.**

Welcome to the new Sleepwell site.

We are in the process of transforming Sleepwell's content, tools, and recommendations for getting your sleep back without medications.

www.sleepwell.ca/





LESS SEDATIVES FOR YOUR OLDER RELATIVES.

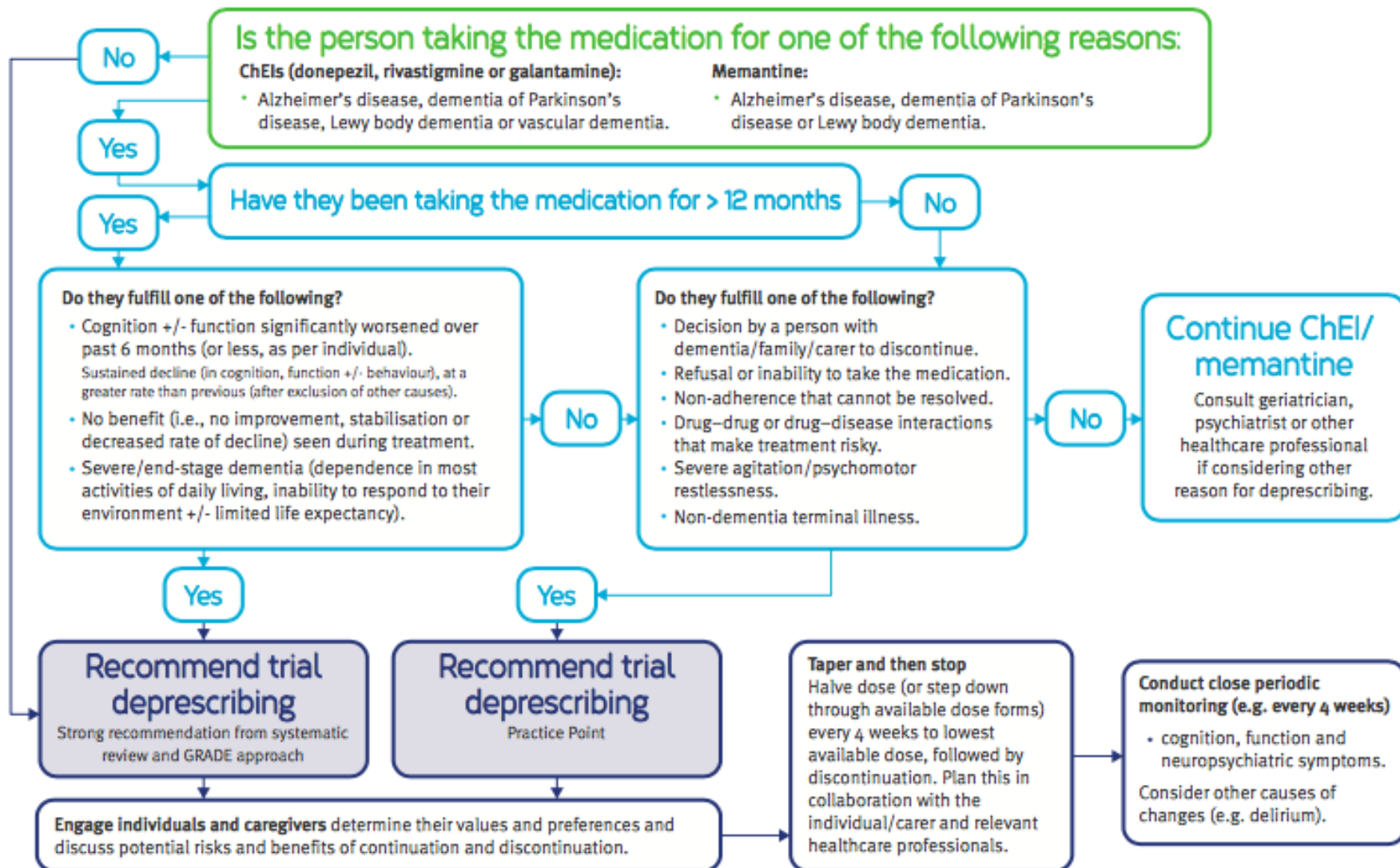
**A toolkit for reducing inappropriate use of
benzodiazepines and sedative-hypnotics
among older adults in hospitals**

version 1.1

Use deprescribing algorithms

Available for:

- Cholinesterase inhibitors and memantine
- PPIs
- Benzodiazepine receptor agonists
- Antihyperglycemics
- Antipsychotics



Monitoring during tapering and after discontinuation

Timing of symptoms after dose reduction/discontinuation	Types of symptoms	Action to be taken by family/nurses/care staff	Possible cause*
Less than 1 week	Severe symptoms, including agitation, aggression, hallucinations or reduced consciousness	Restart previous dose immediately and contact responsible healthcare professional as soon as possible	Adverse drug withdrawal reaction
2 to 6 weeks	Worsening of cognition, behavioural or psychological symptoms or function	Contact responsible healthcare professional and consider restarting previous dose and/or make an appointment to see responsible healthcare professional at the next available time	Re-emergence of symptoms that were being treated by ChEI/memantine
6 weeks to 3 months	Worsening of cognition, behavioural or psychological symptoms or function	Contact responsible healthcare professional at the next available time to make an appointment	Likely progression of condition or possible re-emergence of symptoms that were being treated by ChEI/memantine
> 3 months	Any	As per usual care	Progression of condition

- * Exclude other causes of change in condition (e.g. infection or dehydration) first.
- Discuss monitoring plan with the individual/family/carer and write it down for them (e.g. frequency and type of follow-up). Ensure they have a way to contact a clinician if needed.

Engaging individuals and family/carers

Determining suitability for deprescribing

- Discuss treatment goals – what do they value the most (cognition, quality of life, remaining independent)?
- Ask about experience with dementia symptoms when treatment started and over last 6 months.
- Ask about side effects.

Helping the individual and family/carers to make an informed decision

- Deprescribing is a trial – medication can be restarted if appropriate.
- There are uncertain benefits and harms to both continuing and discontinuing the medication.
- Tailor discussion about benefits and harms to the individual.
- Explore fears and concerns about deprescribing.
- Consider medication costs and local reimbursement/subsidisation criteria.
- If the recommendation to deprescribe is being made due to progression of dementia, remind family/carers that the person with dementia may continue to decline after deprescribing, and explain why.

Non-pharmacological management and ongoing care after deprescribing

See (<http://sydney.edu.au/medicine/cdpc/resources/dementia-guidelines.php>) for Australian guidelines on care of people with dementia, including behavioural and psychological symptoms.

ChEI and memantine availability (Australia)

Drug	Strength
Donepezil (Aricept [®] , Aridon [®] , Arazil [®])	Tablet – 5mg, 10mg
Galantamine (Galantyl [®] , Gamine XR [®] , Reminyl [®])	Controlled release capsule – 8mg, 16mg, 24mg
Rivastigmine (Exelon [®])	Capsule – 1.5mg, 3mg, 4.5mg, 6mg Patch – 4.6mg/24 hours, 9.5mg/24 hours, 13.3mg/24 hours
Memantine (Ebixa [®] , Memanxa [®])	Tablet – 10mg, 20mg

ChEI and memantine side effects

- Common: include gastrointestinal effects, dizziness, confusion, headache, insomnia, agitation, weight loss and falls.
- Rare (ChEI): may include urinary, cardiovascular (e.g. bradycardia), pulmonary and dermatological (e.g. Stevens-Johnson syndrome) complications, Pisa syndrome, seizures, gastrointestinal haemorrhage and rhabdomyolysis.
- Lack of evidence of potential harms in complex older adults.



What works

- ✓ Structured medication reviews
- ✓ Plan for rebound symptoms/withdrawal
- ✓ Communication with community providers
- ✓ Education: Patients (EMPOWER), Clinicians



**DO I STILL NEED
THIS
MEDICATION?**

www.deprescribingnetwork.ca

Become a member!

CaDeN
Canadian Deprescribing
Network



ReCaD
Réseau canadien
pour la déprescription

www.deprescribingnetwork.ca

- Subscribe to our newsletter!
- Twitter : @deprescribingnet
- Facebook : @deprescribingnetwork

CaDeN
Canadian Deprescribing
Network



ReCaD
Réseau canadien
pour la déprescription

Questions?

