

Using Medications Wisely: Deprescribing Consideration

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“Starting medications is like the bliss
of marriage, and stopping them is
like the agony of divorce.”

– Doug Danforth

What is Deprescribing?

“The Systematic Process of identifying and discontinuing [or reducing] medication in instance in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient’s care goals, current level of functioning, life expectancy, values and preferences”

Scott IA, Hilmer SN, Reeve E, et al. JAMA Internal Medicine;175:827-34.

Resources for Deprescribing in the Community and Nursing Home Setting

American Geriatrics Society 2019 Updated AGS Beers Criteria[®] for Potentially Inappropriate Medication Use in Older Adults

*By the 2019 American Geriatrics Society Beers Criteria[®] Update Expert Panel**

See related editorial by Steinman et al. in this issue.

INTENT OF CRITERIA

The primary target audience for the AGS Beers Criteria[®] is practicing clinicians. The criteria are intended for use in adults 65 years and older in all ambulatory, acute, and institutionalized settings of care, **except for the hospice and palliative care settings**. Consumers, researchers, pharmacy benefits managers, regulators, and policymakers also widely use the AGS Beers Criteria[®]. The intention of the AGS Beers Criteria[®] is to improve medication selection; educate clinicians and patients; reduce adverse drug events; and serve as a tool for evaluating quality of care, cost, and patterns of drug use of older adults.

STOPP/START criteria for potentially inappropriate prescribing in older people: version 2

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STOPPFrail (Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy): consensus validation

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Medications to Consider Deprescribing

1. Anticholinergics
2. Benzodiazepines
3. Antipsychotics
4. Anti-dementia medications

1. Anticholinergics

Used for:

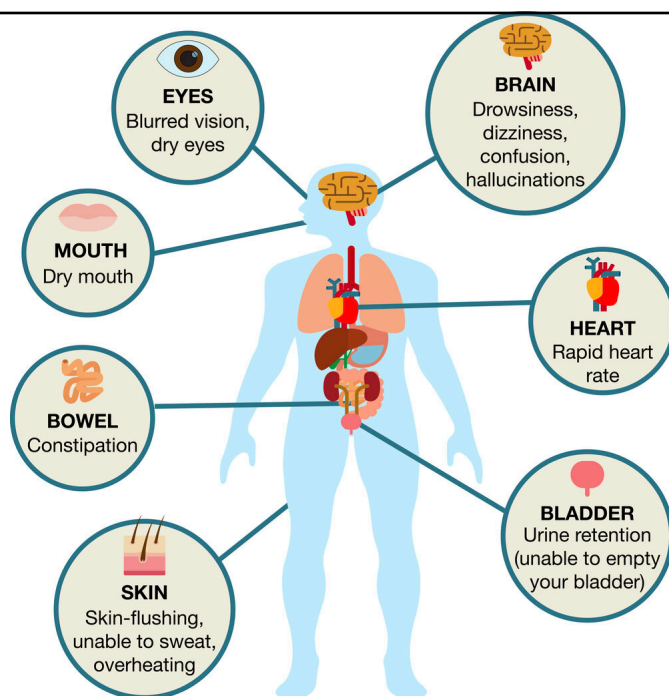
Allergies (anti-histamines)

Parkinson's disease

Urinary incontinence

Psychiatric disorders
(antipsychotics)

....so much more



Collamati A, et al. Aging Clin Exp Res. 2016. 28:25-35.

Anticholinergic and Aging

- Blood-brain barrier permeability changes
- Delayed or slowed metabolism
- Reduced drug elimination
- Changes in cholinergic transmission
- More drug-drug interactions

Collamati A, et al. Aging Clin Exp Res. 2016. 28:25-35.

Anticholinergics and Cognition: The Evidence

- Anticholinergics are associated with worsening cognition in:
 - Community dwelling OAs
 - Institutionalized OAs
 - OAs with disabilities
- Anticholinergics are also associated with **delirium**
- Those with comorbid psychiatric conditions may be more vulnerable
- Up to 50% of those on acetylcholinesterase inhibitors is also taking a drug with anticholinergic properties

Collamati A, et al. Aging Clin Exp Res. 2016. 28:25-35.
Salahudeen MS, et al. BMC Geriatrics. 2015;15(1).
OAs, older adults

Anticholinergic Effects are Cumulative

- Chronic use of anticholinergics is associated with risk of cognitive impairment and dementia
 - Reduced MMSE scores
 - Incident dementia
- The evidence on discontinuation benefits on cognition are conflicting
- Anticholinergics are also associated with:
 - Worsening physical functioning
 - Increased mortality risk
 - Hospitalization risk

Fox C, et al. J Am Geriatr Soc. 2011;59(8):1477-83.
 Pasina L, et al. Drugs Aging. 2013;30(2):103-12.
 Gray SL, et al. JAMA Intern Med. 2015;175(3):401-7.
 Boustani M, et al. J Hosp Med. 2010;5(2):69-75.
 Carnahan RM, et al. 2006;46(12):1481-6.
 MMSE, Mini-Mental State Exam

Anticholinergic Cognitive Burden Scale (ACB)

Drugs with ACB Score of 1

Generic Name	Brand Name
Alimemazine	Theralene™
Alverine	Spasmonal™
Alprazolam	Xanax™
Anipiprazole	Abilify™
Axmapine	Saphris™
Atenolol	Tenormin™
Bupropion	Wellbutrin™, Zyban™
Captopril	Capoten™
Cefixime	Zyfix™
Chlorthalidone	Diuril™, Hygroton™
Cimetidine	Tagamet™
Cidinium	Librax™
Clonazepam	Tranexone™
Codine	Contin™
Colchicine	Colcrys™
Desloratadine	Clarinex™
Diazepam	Valium™
Digoxin	Lanoxin™
Dipyridamole	Persantine™
Disopyramide	Norpace™
Fentanyl	Duragesic™, Actiq™
Furosemide	Lasix™
Fluoxetine	Luvox™
Haloperidol	Halidol™, Haldol™
Hydralazine	Apresoline™
Hydrocortisone	Cortel™, Cortaid™
Iloperidone	Fanapt™
Iscosorbide	Iscord™, Ismo™
Levetiracetam	Keppra™
Loperamide	Immodium™, others
Lorazepam	Claritin™
Mefenbrofenol	Lopressor™, Toprol™
Morphine	MS Contin™, Avages™
Nifedipine	Procardia™, Adalat™
Paliperidone	Invega™
Prednisone	Deltasone™, Sterapred™
Quindine	Quinaglate™
Ranitidine	Zantac™
Risperidone	Risperdal™
Thiophylline	Theodur™, Uniphyll™
Trasolone	Deseryl™
Triamterene	Dyrenium™
Venlafaxine	Effexor™
Warfarin	Coumadin™

Drugs with ACB Score of 2

Generic Name	Brand Name
Amantadine	Symmetrel™
Belladonna	Multiple
Carbamazepine	Tagretol™
Cyclobenzaprine	Flexeril™
Luxamine	Luxitane™
Mepredine	Demerol™
Methotrimeprazine	Levoprome™
Molindone	Moban™
Nefopam	Nefogesis™
Oxcarbazepine	Trileptal™
Pemoline	Drap™

Drugs with ACB Score of 3

Generic Name	Brand Name
Amiripryline	Elavil™
Amoxapine	Asendin™
Atropine	Sal-Tropine™
Benztropine	Cogentin™
Brompheniramine	Dimetapp™
Carbamazepine	Histex™, Carbitas™
Chlorpheniramine	Chlor-Trimeton™
Chlorpromazine	Thorazine™
Clemastine	Tavist™
Clomipramine	Anafranil™
Clozapine	Clozaril™
Darifenacin	Enablex™
Desipramine	Norpramin™
Dicyclanide	Bentyl™
Dimenhydrinate	Dramamine™, others
Diphenhydramine	Benadryl™, others
Doxepin	Sinequan™
Doxylamine	Unisom™, others
Fesoterodine	Toviaz™
Flavoxate	Unipas™
Hydroxyzine	Atarax™, Vistaril™
Hyoscyamine	Anaspaz™, Levsin™
Imipramine	Tofranil™
Medicine	Activest™
Methocarbamol	Robax™
Nortriptyline	Pamelor™
Olanzapine	Zyprexa™
Orphenadrine	Norflex™
Quetiapine	Seroquel™
Paroxetine	Paxil™
Perphenazine	Trifluon™
Propiomazine	Phenazag™
Propamethazine	Pro-Banthine™
Propiverine	Detrol™
Quetiapine	Seroquel™
Scopolamine	Transderm Scop™
Sulfonamide	Yescare™
Thioridazine	Mellaril™
Tolterodine	Detrol™
Trifluoperazine	Stelazine™
Trihexyphenidyl	Artane™
Trimipramine	Surmontil™
Tropium	Sanctura™

Categorical Scoring:

- Possible anticholinergics include those listed with a score of 1; Definite anticholinergics include those listed with a score of 2 or 3

Numerical Scoring:

- Add the score contributed to each selected medication in each scoring category
- Add the number of possible or definite Anticholinergic medications

Notes:

- Each definite anticholinergic may increase the risk of cognitive impairment by 46% over 6 years.³
- For each on point increase in the ACB total score, a decline in MMSE score of 0.33 points over 2 years has been suggested.⁴
- Additionally, each one point increase in the ACB total score has been correlated with a 26% increase in the risk of death.⁴

Aging Brain Care

www.agingbraincare.org

Boustani M, et al. J Hosp Med. 2010;5(2):69-75.

Anticholinergic Deprescribing

DEPRESCRIBING GUIDE FOR ANTICHOLINERGIC DRUGS FOR PARKINSONISM

(including benztropine [bentropine], trihexyphenidyl [benzhexol], biperiden)

i This guide provides deprescribing information that can be applied to written and/or verbal communication (in the form of "preferred language") between clinicians, patients and/or carers. Adapt appropriately for individual patients.

CONSIDER TWO STEPS
WHEN DEPRESCRIBING:

Show

DEPRESCRIBING GUIDE FOR ANTICHOLINERGIC DRUGS FOR URINARY INCONTINENCE (ANTIMUSCARINICS)

(including oxybutynin, solifenacin, tolterodine, darifenacin, propantheline)

i This guide provides deprescribing information that can be applied to written and/or verbal communication (in the form of "preferred language") between clinicians, patients and/or carers. Adapt appropriately for individual patients.

CONSIDER TWO STEPS
WHEN DEPRESCRIBING:

1 Should I deprescribe?

GO TO SECTION:

Indication
How to wean
Alternative management
Monitoring
Evidence-based advice
Summarised phrasing during admission and/or at discharge
References

2 How do I deprescribe?

NSW
TAG

NSW
Therapeutic
Advisory
Group Inc.

2. Benzodiazepines

Benzodiazepines: The Evidence

- Benzodiazepines for insomnia
 - Efficacy diminishes ~ week 4
 - AE persist
- Conflicting evidence
- A 2016 SR and MA (n=3,696) found a strong association between BZD and dementia
- Memory loss, confusion and disorientation significantly more common
- BZD associated with retrograde amnesia
 - Persistent amnestic effects

Islam MM, et al. Neuroepidemiology. 2016; 47(3-4): 181-91.

Glass J, et al. BMJ. 2005;331(7526):1169

Vinkers CH, et al. Adv Pharmacol Sci. 2012;2012:416864

AE, adverse effects; SR, systematic review; MA, meta-analysis; BZD, benzodiazepine

Who Should be Deprescribed?

- Chronic insomnia management (> 4 weeks)
- Management of anxiety which is otherwise controlled
 - On long-term therapeutic agents
 - Participating in CBT or other therapy
- Limited evidence, not recommended to deprescribe:
 - Restless leg syndrome
 - Uncontrolled anxiety, depression, physical or mental condition causing/aggravating insomnia
 - Alcohol withdrawal

Pottie K, et al. Can Fam Physician. 2018;64(5):339-351.

CBT, cognitive behavioral therapy

Tapering Recommendations

- Consider adding CBT when possible
- Small dose reductions ~25% every 2-4 weeks
- **Do not** switch to a long-acting benzodiazepines
- Monitoring
 - Every 2-4 weeks
 - Sleep quality
 - Anxiety (*may improve*)
 - Other withdrawal symptoms: GI, irritability, sweating
 - Seizures*

*occur rarely, with abrupt cessation of high doses of benzodiazepines or those with underlying seizure disorder
 Pottie K, et al. Can Fam Physician. 2018;64(5):339-351.
 CBT, cognitive behavioral therapy; GI, gastrointestinal

Original Investigation

Reduction of Inappropriate Benzodiazepine Prescriptions Among Older Adults Through Direct Patient Education The EMPOWER Cluster Randomized Trial

Cara Tannenbaum, MD, MSc; Philippe Martin, BSc; Robyn Tamblyn, PhD; Andrea Benedetti, PhD;
Sara Ahmed, PhD

Deprescribing can feasibly be done in the community with as little additional effort as mailing a flyer to your patient!

27% of participants receiving the intervention discontinued their BZD within 6 months (NNT= 5)

Tannenbaum C, et al. JAMA Intern Med. 2014;174(6):890-8.
 NNT, number needed to treat; BZD, benzodiazepine



You May Be at Risk

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

Available here: <http://www.criugm.qc.ca/fichier/pdf/BENZOeng.pdf>

QUIZ

Sedative-hypnotic medication

1. The medication I am taking is a mild tranquilizer that is safe to take 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

Available here: <http://www.criugm.qc.ca/fichier/pdf/BENZOeng.pdf>

Ask yourself yes or no?

Have you been taking your medication for a while?

☐ Y ☐ N

Are you often tired and sleepy during the day?

☐ Y ☐ N

Do you ever feel hungover in the morning, even though you have not been drinking?

☐ Y ☐ N

Do you ever have problems with your memory or your balance?

☐ Y ☐ N

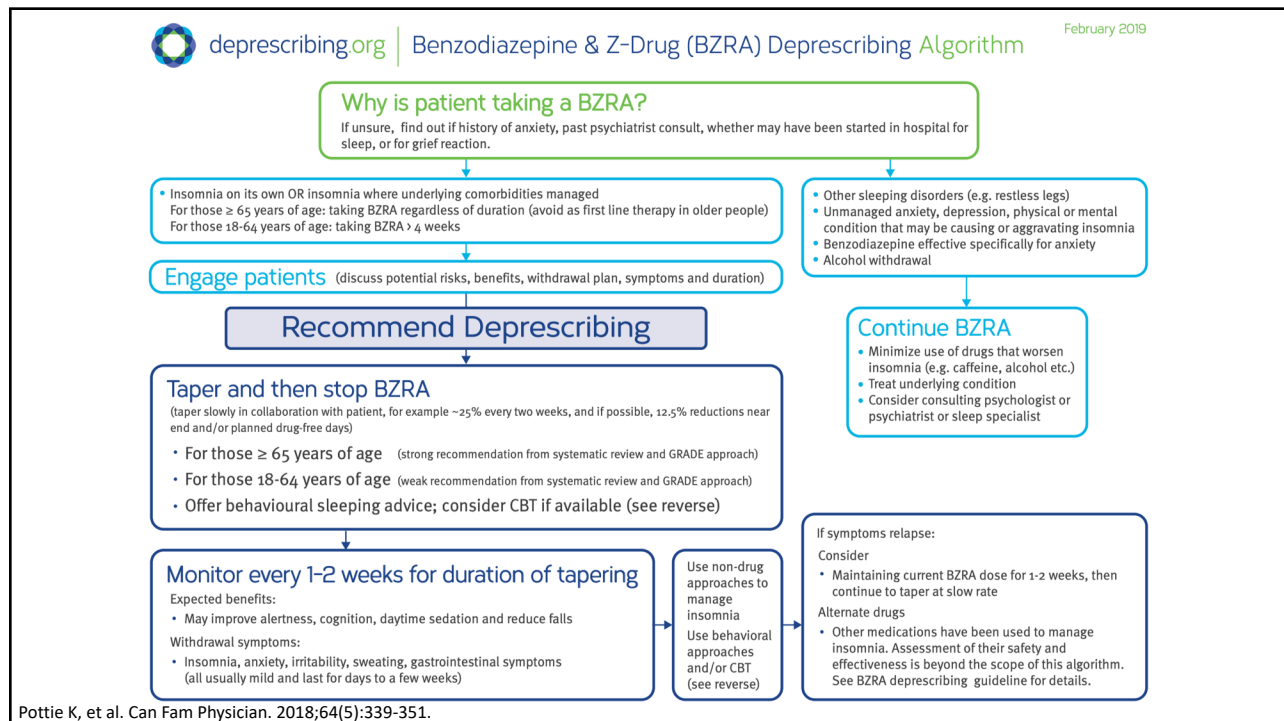
Available here: <http://www.criugm.qc.ca/fichier/pdf/BENZOeng.pdf>

Tapering-off program

Be sure to talk to your doctor, nurse or pharmacist before you try reducing your dose or stopping your medication.

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								

Available here: <http://www.criugm.qc.ca/fichier/pdf/BENZOeng.pdf>



Deprescribing Medications Used for Dementia and Behavioral Symptoms

3. Antipsychotic Medications

Antipsychotics: Candidates for Deprescribing

- Management of behavioral and psychological symptoms of dementia (BPSD)
 - > 3 months
- Insomnia
- Evidence to support **against** deprescribing:
 - Schizophrenia, schizoaffective disorder
 - Bipolar disorder
 - Acute delirium
 - OCD
 - Alcoholism, cocaine abuse
 - Parkinson's disease psychosis
 - Adjunct management of depression

Bjerre LM, et al. Can Fam Physician. 2018;64(1):17-27.

Antipsychotics: The Evidence

- Limited efficacy for BPSD
- May reduce aggressive behavior
- May reduce caregiver burden (small impact)
 - Caregivers report improved QOL when antipsychotics are *not* used
- Poor efficacy for insomnia management

Schneider LS, et al. Am J Geriatr Psychiatry. 2006;14(3):191-210.

Ma H, et al. J Alzheimers Dis. 2014;42(3):915-37.

Adelman RD, et al. JAMA. 2014;311(10):1052-9.

Mohamed S, et al. J Clin Psychiatry. 2012;73(1):121-8.

BPSD, behavioral and psychological symptoms of dementia; QOL, quality of life

Antipsychotics: Potential Harm

- Metabolic symptoms
- EPS
- Falls, hip fractures
- Somnolence
- Anticholinergic symptoms
- Increased risk of:
 - Death
 - Cerebrovascular events

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA *See full prescribing information for complete boxed warning.*

- Atypical antipsychotic drugs are associated with an increased risk of death (5.1)
- Quetiapine is not approved for elderly patients with Dementia-Related Psychoses (5.1)

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS *See full prescribing information for complete boxed warning.*

- Increased risk of suicidal thinking and behavior in children, adolescents and young adults taking antidepressants for major depressive disorder and other psychiatric disorders (5.2)
- SEROQUEL XR is not approved for the treatment of depression, however, an immediate release form of quetiapine (Seroquel) is approved for the treatment of bipolar depression. (5.2)

Ma H, et al. J Alzheimers Dis. 2014;42(3):915-37.

Schneider LS, et al. JAMA. 2005;294(15):1934-43.

Huang AR, et al. Drugs Aging. 2012;29(5):359-76.

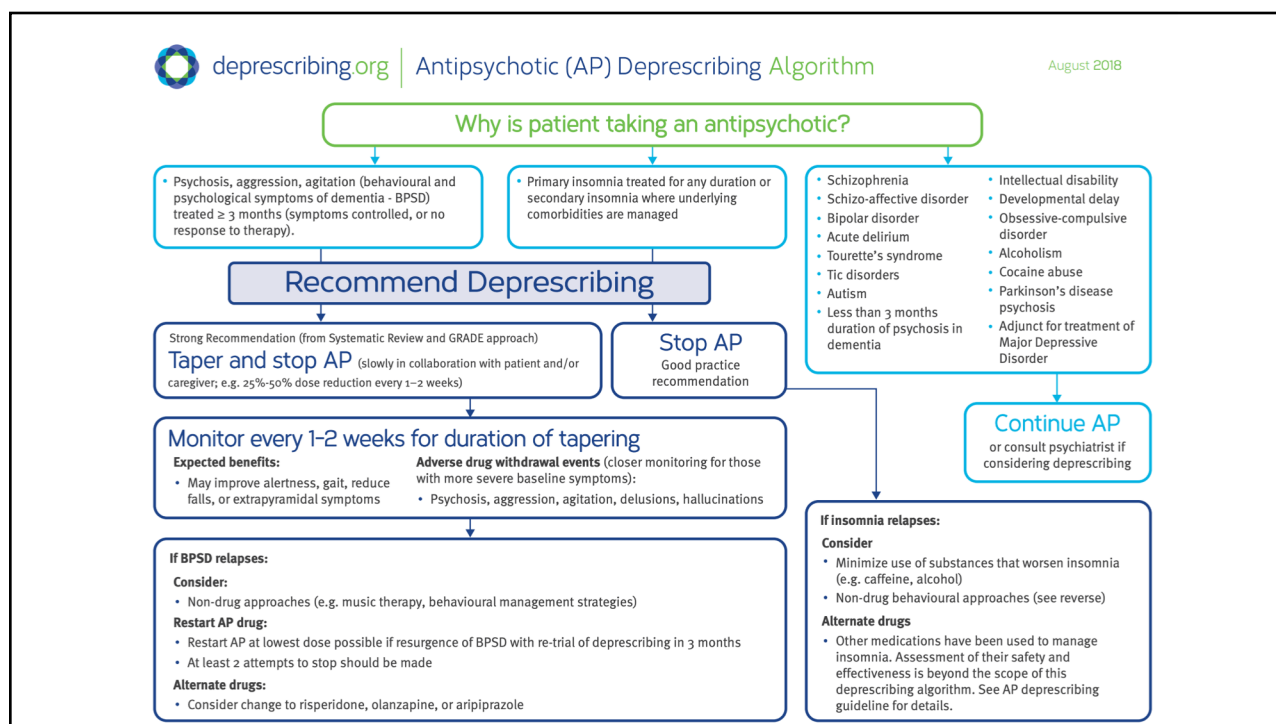
Shah BM, et al. Clin Geriatr Med. 2012;28(2):173-86.

EPS, extrapyramidal symptoms

Antipsychotic Medication Taper

- Reduce dose by 25-50% every 1-2 weeks in those with BPSD
- Can discontinue without taper in setting of insomnia management
- Consider attempting x 2 times before considering failure
- Withdrawal symptoms
 - Rebound insomnia
 - Psychosis
 - Aggression
 - Agitation
 - Delusions
 - Hallucinations

Bjerre LM, et al. Can Fam Physician. 2018;64(1):17-27.



Antipsychotics Tapering: Monitoring and Management

- **Monitoring**
 - Changes in symptoms
 - Worsening behavior
 - Rebound insomnia
 - Every 1-2 weeks, check in with family, patient and caregivers
- **Management of worsening BPSD**
 - If failure, add back in AP (aripiprazole, olanzapine, risperidone preferred)
 - Lowest effective dose
 - Consider taper trial again
 - Non-pharmacological approaches (management of underlying causes)
- **Management of insomnia**
 - Sleep hygiene
 - Pharmacotherapy for insomnia – avoid BZD, non-BZD hypnotics

Bjerre LM, et al. Can Fam Physician. 2018;64(1):17-27.

BZD, benzodiazepines; BPSD, behavioral and psychological symptoms of dementia

Cohen-Mansfield Agitation Scale

	1- Never	2- Less than once a week	3- Once or twice a week	4- Several times a week	5- Once or twice a day	6- Several times a day	7- Several times an hour
Physical/Aggressive							
1. Hitting (including self)	1	2	3	4	5	6	7
2. Kicking	1	2	3	4	5	6	7
3. Grabbing onto people	1	2	3	4	5	6	7
4. Pushing	1	2	3	4	5	6	7
5. Throwing things	1	2	3	4	5	6	7
6. Biting	1	2	3	4	5	6	7
7. Scratching	1	2	3	4	5	6	7
8. Spitting	1	2	3	4	5	6	7
9. Hurting self or others	1	2	3	4	5	6	7
10. Tearing things or destroying property	1	2	3	4	5	6	7
11. Making physical sexual advances	1	2	3	4	5	6	7
Physical/Non-Aggressive							
12. Pace, aimless wandering	1	2	3	4	5	6	7
13. Inappropriate dress or disrobing	1	2	3	4	5	6	7
14. Trying to get to a different place	1	2	3	4	5	6	7
15. Intentional falling	1	2	3	4	5	6	7
16. Eating/drinking inappropriate substance	1	2	3	4	5	6	7
17. Handling things inappropriately	1	2	3	4	5	6	7
18. Hiding things	1	2	3	4	5	6	7
19. Hoarding things	1	2	3	4	5	6	7
20. Performing repetitive mannerisms	1	2	3	4	5	6	7
21. General restlessness	1	2	3	4	5	6	7
Verbal/Aggressive							
22. Screaming	1	2	3	4	5	6	7
23. Making verbal sexual advances	1	2	3	4	5	6	7
24. Cursing or verbal aggression	1	2	3	4	5	6	7
Verbal/Non-aggressive							
25. Repetitive sentences or questions	1	2	3	4	5	6	7
26. Strange noises (weird laughter or crying)	1	2	3	4	5	6	7
27. Complaining	1	2	3	4	5	6	7
28. Negativism	1	2	3	4	5	6	7
29. Constant unwarranted request for attention or help	1	2	3	4	5	6	7

Signature: _____ Date: _____

*The use of this tool is strictly for clinical assessment and educational purposes only and is restricted from use in any for-profit activities. May 2013
Developed by and shared with permission of Interior Health

Bjerre LM, et al. Can Fam Physician. 2018;64(1):17-27.

4. Anti-Dementia Medications

Acetylcholinesterase Inhibitors

Memantine

Anti-Dementia Medications: Role in Therapy

- Studies supporting efficacy of acetylcholinesterase inhibitors and memantine are limited in duration of follow-up
- Delayed nursing home admission
- Improved ADLs, cognition, and neuropsychiatric symptoms
- Delay of symptom progression
- *Improve symptoms but do not alter the course of disease*

Reeve E, et al. Med J Aust. 2019;210(4):174-9.
ADLs, activities of daily living

Anti-Dementia Medications: Deprescribing Candidates

- A trial for deprescribing is recommended for those on
 - Acetylcholinesterase inhibitors for a minimum of 12 months
 - Memantine for a minimum of 12 months
- With the indication of:
 - Alzheimer's disease dementia
 - Dementia of Parkinson's Disease
 - Lewy Body Dementia
- And those with:
 - Significant worsening of cognition and/or functional status over the last 6 months
 - No proven benefit – improvement, stabilization, or decreased rate of decline
 - Severe/end-stage dementia –ADL dependence

Reeve E, et al. Med J Aust. 2019;210(4):174-9.

Deprescribing Dementia Medications: Other Rationales

- Refusal to take medications/non-adherence
- Patient and/or caregivers/family make the decision
- Drug-drug and/or drug-disease interactions
- Severe agitation/psychomotor restlessness
- Non-dementia terminal illnesses

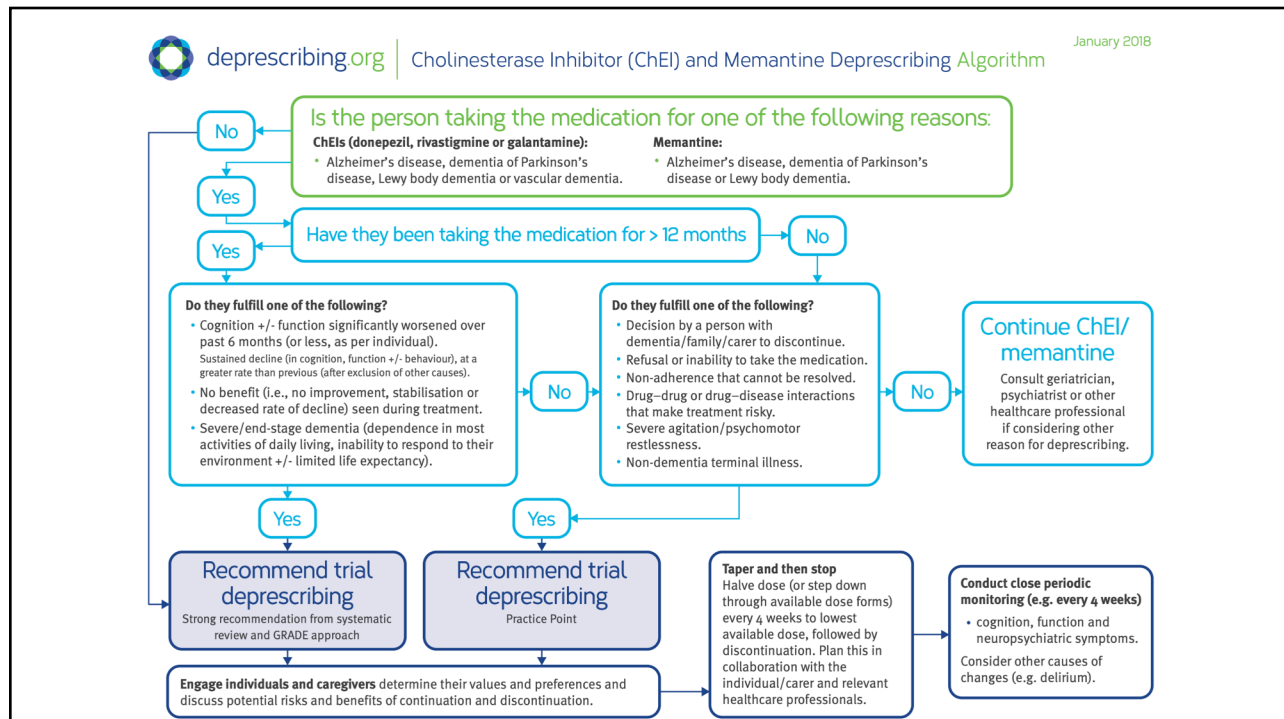
Reeve E, et al. Med J Aust. 2019;210(4):174-9.

Deprescribing Trial

Reducing the dose by 25-50% every 1-4 weeks, or reducing to next possible dose available every 4 weeks

Drug:	Dosages available:	Time for 5 half-lives:
Donepezil (Aricept®)	23 mg daily → 10 mg daily → 5 mg daily	15 days
Galantamine (Razadyne®)	24 mg daily → 16 mg daily → 8 mg daily	2 days
Rivastigmine (Exelon®)	13.3 mg/24 hours → 9.5 mg/24 hours → 4.6 mg/24 hour Or 6 mg BID → 4.5 mg BID → 3 mg BID → 1.5 mg BID → 1.5 mg daily	17 days
Memantine (Namenda®)	20 mg daily (or 10 mg BID) → 10 mg daily	21 days

Reeve F. et al. Med J Aust. 2019;210(4):174-9.



Deprescribing Trial: Monitoring

- Requires close monitoring: minimum every 4 weeks
- Monitoring for:
 - Worsening of cognitive function
 - Worsening of physical functioning/ADLs
 - Withdrawal symptoms (within 3-7 days)
- Managing withdrawal symptoms
 - Re-starting at lowest effective dose
 - Consider anti-dopaminergic agents if in palliative care setting

Reeve E, et al. Med J Aust. 2019;210(4):174-9.
 Kwak YT, et al. Geriatr Gerontol Int. 2009;9(2):203-5.
 ADLs, activities of daily living

Deprescribing Dementia Medications: Talking Points

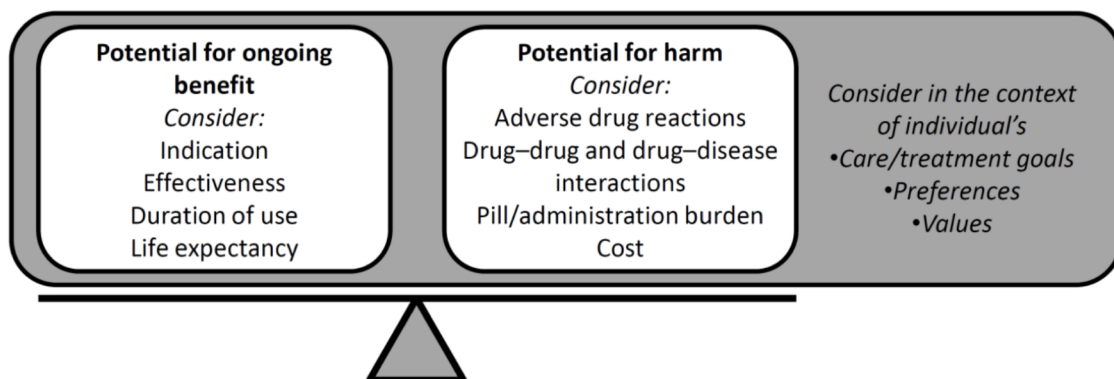
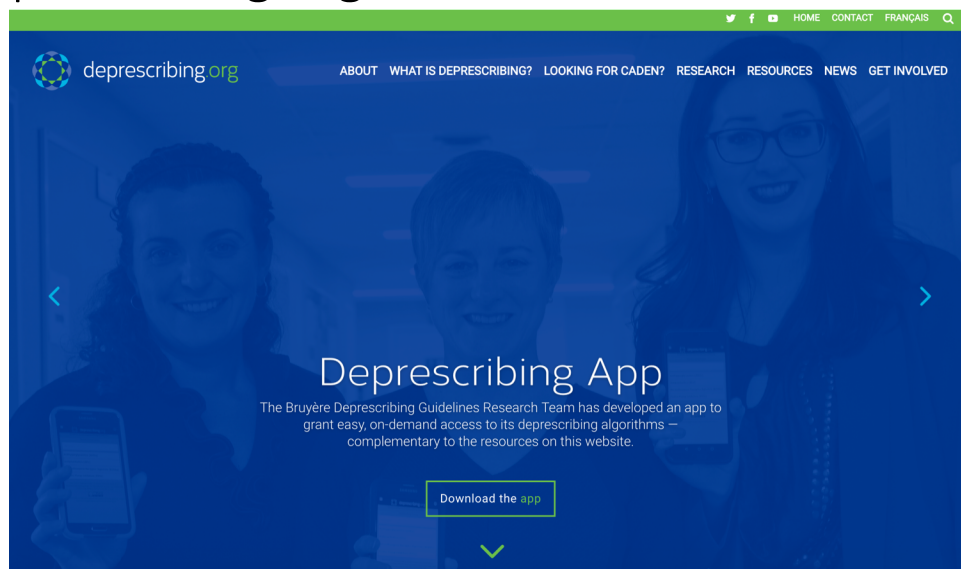


Figure 1: Weighing up the potential benefits and harms of ongoing use of ChEIs and memantine

Reeve E, et al. Med J Aust. 2019;210(4):174-9.

Additional Tools

Deprescribing.org



Questions?

Email:

sspringer1@une.edu

