Using Medications Wisely: Deprescribing Consideration
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Assistant Professor
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7 April 2021

“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 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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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

Anticholinergic and Aging

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


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

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


**Anticholinergic Cognitive Burden Scale (ACB)**


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**Categorical Scoring**
- Possible anticholinergics include those listed with a score of 2 or 3

**Numerical Scoring**
- Add the score contributed to each anticholinergic 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 40% over 3 years.
- For each one point increase in the ACB total score, a decline in MMSE score of 0.30 points over 2 years has been suggested.
- Additionally, each one-point increase in the ACB total score has been associated with a 2% increase in the risk of death.
Anticholinergic Deprescribing

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

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

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


CBT, cognitive behavioral therapy; GI, gastrointestinal

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)


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

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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/BENZ0Eng.pdf](http://www.criugm.qc.ca/fichier/pdf/BENZ0Eng.pdf)

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Tapering-off program

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

<table>
<thead>
<tr>
<th>WEEKS</th>
<th>TAPERING SCHEDULE</th>
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Available here: [http://www.criugm.qc.ca/fichier/pdf/BENZ0Eng.pdf](http://www.criugm.qc.ca/fichier/pdf/BENZ0Eng.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

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

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

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

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

Cohen-Mansfield Agitation Scale

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<th>Physical/Non-Aggressive</th>
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<td>12. Face, unless avoiding</td>
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<td>14. Forgetting to go to a different place</td>
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<td>16. Eating/drinking inappropriate substance</td>
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<td>17. Hanging things improperly</td>
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<td>20. Screaming</td>
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<td>22. Cursing or verbal aggression</td>
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<td>23. Reassuring statements or questions</td>
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<td>24. Strange noises (audible laughter or crying)</td>
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<td>25. Complaining</td>
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<td>26. Regulating</td>
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<td>27. Constant unattended request for attention or help</td>
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Instructions:

Cohen-Mansfield Agitation Inventory (CMAI)

Name: ____________________________

For each of the behaviors below, check the rating that indicates the average frequency of occurrence over the last 2 weeks.

- Never
- Short once a week
- Once or twice a week
- Several times a week
- Once or twice a day
- Several times a day
- Once or twice an hour
- Several times an hour

- This use of this tool is strictly for clinical assessment and educational purposes only and is restricted from use in any for-profit activities.


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

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


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

Deprescribing Trial

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

<table>
<thead>
<tr>
<th>Drug:</th>
<th>Dosages available:</th>
<th>Time for 5 half-lives:</th>
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<tbody>
<tr>
<td>Donepezil (Aricept®)</td>
<td>23 mg daily → 10 mg daily → 5 mg daily</td>
<td>15 days</td>
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<tr>
<td>Galantamine (Razadyne®)</td>
<td>24 mg daily → 16 mg daily → 8 mg daily</td>
<td>2 days</td>
</tr>
<tr>
<td>Rivastigmine (Exelon®)</td>
<td>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</td>
<td>17 days</td>
</tr>
<tr>
<td>Memantine (Namenda®)</td>
<td>20 mg daily (or 10 mg BID) → 10 mg daily</td>
<td>21 days</td>
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**deprescribing.org** | Cholinesterase Inhibitor (ChEI) and Memantine Deprescribing Algorithm | January 2018

**Is the person taking the medication for one of the following reasons?**
- Alzheimer's disease, dementia of Parkinson's disease, Lewy body dementia or vascular dementia.
- Memantine:
  - Alzheimer's disease, dementia of Parkinson's disease or Lewy body dementia.

**Have they been taking the medication for > 12 months?**
- No
  - Do they fulfill one of the following?
    - Cognition +/- function significantly worsened over past 6 months (or less, as per individual).
    - Sustained decline in cognition, function +/- behavior, at a greater rate than previous (other exclusion of other cause).
    - No benefit (i.e., no improvement, stabilization or decreased rate of decline) seen during treatment.
    - Severe/end-stage dementia (dependence in most activities of daily living, inability to respond to their environment +/- limited life expectancy).
    - Yes
    - Recommend trial deprescribing
    - Strong recommendation from systematic review and GRADE approach
    - Recap and individual and caregiver determine their values and preferences and discuss potential risks and benefits of continuation and discontinuation.

- Yes
  - Continue ChEI/memantine
    - Consult geriatrician, psychiatrist or other healthcare professional if considering other reason for deprescribing.

**Taper and then stop**
- Halve dose (or step down through available dose forms) every 4 weeks to lowest available dose, followed by discontinuation. Plan this in collaboration with the individual/career and relevant healthcare professionals.

- Conduct close periodic monitoring (e.g. every 4 weeks)
  - Cognition, function and neuropsychiatric symptoms.
  - Consider other causes of changes (e.g. delirium).
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

ADLs, activities of daily living

Deprescribing Dementia Medications: Talking Points

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

Additional Tools

Deprescribing.org
Medstopper

MedStopper is a deprescribing resource for healthcare professionals and their patients.

1. Frail elderly?
2. Generic or Brand Name:
3. Select Condition Treated:

MedStopper Plan

Arrange medications by: Stopping Priority

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<tr>
<td>RED=Highest</td>
<td>gliclazide (Gluco lone ) / Metformin / type 2 diabetes</td>
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<td>Tapering not required</td>
<td>symptoms of increased thirst/diabetes, re-measure A1c in 3 months, measure blood glucose only if high glucose symptoms occur</td>
<td>None</td>
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<tr>
<td>GREEN =Lowest</td>
<td>ASA (Aspirin) / ASA / previous heart attack or stroke</td>
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<td>Tapering not required</td>
<td>None</td>
<td>Details</td>
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<td>YELLOW</td>
<td>atenolol (Betaxolol) / Beta blockers / previous heart attack or stroke</td>
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<td></td>
<td>Tapering not required</td>
<td>None</td>
<td>None</td>
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Questions?

Email: sspringer1@une.edu