Deprescribing at the End of Life: When Less is More

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Objectives

- Discuss goals of and barriers to deprescribing
- Present strategies for deprescribing medications at end of life
- Review common medication classes to target for deprescribing and pharmacological considerations
- Highlight tools and resources to aid in deprescribing
Case: Miss Mary

- 85 y/o F with coronary artery disease, Type II diabetes, atrial fibrillation with moderate dementia was discharged from hospital after a stroke to a long term care facility with hospice.

- Has difficulty swallowing but able to tolerate modified diet and crushed pills
- Can perform most basic activities of daily living (eating, mobility, self care)
- Needs assistance with more advanced cares
Starting Drug Count: 15
Pills per day: 20

Miss Mary’s (non Hospice) Medications

• Cardiac
  • Aspirin 81 mg daily
  • Clopidogrel 75 mg daily
  • Warfarin 2 mg daily
  • Metoprolol 50 mg BID
  • Lisinopril 10 mg daily
  • Atorvastatin 20 mg nightly

• Post-stroke seizure prophylaxis
  • Levetiracetam 500 mg BID

• Gastroenterology protection
  • Pantoprazole 40 mg daily

• Dementia
  • Donepezil 10 mg daily
  • Memantine 5 mg BID

• Diabetes
  • Metformin 1000 mg BID
  • Glipizide XL 10 mg daily

• Bone Health
  • Alendronate 70 mg weekly
  • Calcium + D 600 mg/200 units BID

• Other
  • Ocuvite 1 tab daily
• Family is interested in reducing pill burden

• They ask you to review her list and reduce or stop any medications you think appropriate

• Where do you start???
Discussion Road Map

• Who are we targeting?
• Why deprescribe?
• Barriers to deprescribing
• Low hanging fruit – Medications that DO NOT need to be tapered/weaned
• Medications that DO need tapering/weaning
• Common medications that need dose reductions
What population are we focusing on today?

- Focus on patients who are suspected to have long weeks to months
  - Not patients with hours to days

- Still relatively functional and able to take medications by mouth

- Patient who want to minimize their bill burden at any point in their illness
Why deprescribe? What’s the harm?

- Polypharmacy correlates with increased
  - Drug interactions
  - Adverse events
  - Hospitalization and mortality
  - Medication Costs
  - Pill Burden

- Age and disease related pharmacokinetic changes = Increased drug exposure
  - Altered renal and hepatic function
  - Decreased nutritional status, altered protein binding

Masnoon N, et al. BMC geriatrics 2017
Reeve E, et al. Drugs Aging 2013
Burden of Polypharmacy Near End of Life

- Patients discharged to nursing facility average 14 +/- 4.7 medications

- Journal Pain and Symptom Management 2016:
  - 11.5 +/- 5 medications for primary disease prevention in last month-1 year of life

- Retrospective review of 4252 patients enrolled in hospice in 11 US states in 2010
  - Average 7.9 PRN medications, 8.3 scheduled medications
  - Most common 6 were those prescribed upon admission in the comfort kits
    - Acetaminophen, morphine, haloperidol, lorazepam, prochlorperazine, and atropine
How do you identify which medications are appropriate to deprescribe?

- Benefits no longer outweigh risk of adverse effects
- Time to benefit is longer than anticipated life expectancy
- Treatment target no longer aligns with patient’s goals of care

- Deprescribing is a trial – medications can be restarted!!!
But I didn’t start this medication!

Common Barriers to Deprescribing

• Lack of provider confidence

• Fear of triggering psychological distress from patient

• Patient psychological attachment to chronic medications

• Patient/family not understanding their prognosis
The guidelines say my patient needs this...

- American Diabetic Association
  - Insulin, Metformin, Sulfonylureas

- JNC 8, ACC/AHA STEMI guidelines
  - Beta blockers, ACE inhibitors, diuretics, aspirin

- CHEST Guidelines for VTE
  - Warfarin, Enoxaparin, DOACs

- ATP III, ACC/AHA Guidelines for Cholesterol
  - Statins, fenofibrates, niacin

- AACE/ACE Osteoporosis and Hypothyroidism
  - Bisphosphonates, Levothyroxine

- GOLD guidelines for COPD
  - Inhaled steroids, bronchodilators, anticholinergics

- APA guidelines for Major Depressive Disorder or Agitation/Psychosis in patients with Dementia
  - Antidepressants, antipsychotics

Where are the deprescribing guidelines???
Easy targets for discontinuation

- Vitamins, Multivitamins, Antioxidants
  - Calcium and vitamin D: changes in bone mineral density and prevention of osteoporosis irrelevant at end of life
    - Continue in patients on bone modifying agents for oncology indications

- Supplements
  - Iron: anemia of chronic disease often misdiagnosed as iron deficiency
  - Complementary medicines: lack data for clinical benefit, often have interactions with other medications

- Bisphosphonates
  - Risks of esophagitis outweighs any continued benefit

Easy targets for discontinuation

- Docusate
  - Poor evidence for efficacy in the management of constipation
  - 74 patients randomized to receive Docusate 200 mg BID + Senna vs Placebo + Senna in 3 Canadian inpatient hospice facilities
    - No significant differences in stool volume, frequency, or consistency between docusate and placebo
    - Additional interventions to manage constipation were required in both arm in approximately 70% of patients (no different)
    - Use may be considered on case by case basis

The statin can go!

- Evaluation of risks and benefits of statin use at the end of life
- Randomized 381 patients with life expectancy 1 month to 1 year to continue vs discontinue statin therapy
  - No difference in 60 day mortality
  - No difference in cardiovascular events
  - QOL better in the discontinuation arm
  - Daily cost savings of $3.37 ($716 annually)

- Can extrapolate to other anti-lipid agents: niacin, fibrates, omega-3

What about those eye drops?

- American Glaucoma Society 2016 Annual Meeting:
  - 214 patients, primary open angle glaucoma treated with prostaglandin >6 months
  - 124 assigned to discontinue and washout
  - Average IOP at baseline 26.6mmHg (normal 12-22mmHg)
  - Average IOP with treatment 14.5mmHg
  - After 6 weeks without treatment, average IOP 20.3mmHg

- If eye pain, redness, blurry vision resume drops!!!
Antiplatelet agents

- Clopidogrel (Plavix®), Ticagrelor (Brilinta®), Prasugrel (Effient®)
  - Recommended duration of therapy only 12 months after ACS/PCI
    - Discontinuation often missed

- Aspirin
  - ACS Guidelines recommend indefinite treatment for secondary prevention
    - Assess clinical significance near end of life
  - Updated 2019 CVD primary prevention guidelines no longer recommend low dose aspirin

- Overall bleeding risks > long-term benefit, especially in elderly

Arnett DK, et al. Journal of the American College of Cardiology. 2019
To anticoagulate...

• No guidelines for discontinuation, but duration of therapy differs by indication
  • VTE: Chest guidelines = 3 months
  • Cancer-associated VTE: no consensus, common 3-6 months
  • Indefinite treatment for Afib and mechanical valves

• Consider alternatives to Warfarin if anticoagulation needed/desired
  • Difficult to manage with altered dietary intake and liver function at end of life, requires INR monitoring
  • Assess renal dosing needs for LMWH or direct oral anticoagulants

Lee AYY. Blood 2017
January CT, #278 Warfarin And Palliative Care. Web. 26 Feb. 2015
... Or Not?

- Discontinue anticoagulation if
  - Recommended duration of treatment has been met
  - Risk of bleed, falls outweighs risk of thrombosis

- Consider patient and family wishes
Miss Mary’s Updated Medication List

- **Cardiac**
  - Aspirin 81 mg daily
  - Clopidogrel 75 mg daily
  - Warfarin 2 mg daily
  - Metoprolol 50 mg BID
  - Lisinopril 10 mg daily
  - Atenolol 25 mg nightly

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  - Memantine 5 mg BID

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  - Glipizide XL 10 mg daily

- **Bone Health**
  - Alendronate 70 mg weekly
  - Calcium + D 600 mg/200 units BID

- **Other**
  - Ocuvite 1 tab daily

**Drug Count:** 15

**Pills per day:** 20
# Drugs requiring tapering

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Disease Recurrence</th>
<th>Withdrawal</th>
<th>Rebound</th>
<th>Clinical Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha Blockers</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Agitation, headache, hypertension, palpitations</td>
</tr>
<tr>
<td>ACE Inhibitors/ARBs</td>
<td>✓</td>
<td></td>
<td></td>
<td>Heart failure, hypertension</td>
</tr>
<tr>
<td>Antianginals</td>
<td>✓</td>
<td></td>
<td></td>
<td>Angina</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Anxiety, depression, seizures</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Anxiety, chills, depression, GI disturbance, headache, insomnia, irritability, malaise, myalgia</td>
</tr>
<tr>
<td>Antiparkinsons</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Hypotension, psychosis, rigidity, tremor</td>
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<tr>
<td>Antipsychotics</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Dyskinesias, insomnia, nausea, restlessness</td>
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<tr>
<td>Anticholinergics</td>
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<td></td>
<td></td>
<td>Anxiety, nausea, headache, dizziness</td>
</tr>
<tr>
<td>Baclofen</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Agitation, anxiety, confusion, depression, hallucinations, hypertonia, mania, nightmares, paranoia, seizures</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>Agitation, anxiety, confusion, delirium, insomnia, seizures</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Angina, anxiety, hypertension, ACS, tachycardia</td>
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<tr>
<td>Corticosteroids</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>Anorexia, hypotension, nausea, weakness, adrenal insufficiency, inflammatory response</td>
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<tr>
<td>Digoxin</td>
<td>✓</td>
<td></td>
<td></td>
<td>Heart failure, palpitations</td>
</tr>
<tr>
<td>Diuretics</td>
<td>✓</td>
<td></td>
<td></td>
<td>Heart failure, hypertension</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>✓</td>
<td></td>
<td></td>
<td>Pain recurrence</td>
</tr>
<tr>
<td>Opioids</td>
<td>✓</td>
<td></td>
<td></td>
<td>Abdominal cramping, agitation, anger, anxiety, chills, diaphoresis, diarrhea, insomnia</td>
</tr>
</tbody>
</table>

Adapted from: Scott IA, et al. Evid Based Med 2013
Diabetes and end of life goals: ADA guidance

- Stable patients: continue current regimen with less stringent glucose control

- Promote comfort and quality of life
  - Discontinue A1C monitoring and minimize finger sticks

- Patients with organ failure: avoid hypoglycemia
  - Type II: taper or discontinue agents likely to cause hypoglycemia
  - Type I: adjust insulin according to food intake

- Dying patients: minimize acute complications
  - Type II: discontinuation of all agents reasonable
  - Type I: consider low dose basal insulin

American Diabetes Association. Diabetes Care 2018
Adjusting and stopping hypoglycemic agents

- Drugs most likely to cause hypoglycemia: stop or reduce dose
  - Sulfonylureas: long acting agents (glimepiride, glyburide, glipizide XL) increase risk over shorter acting agents (glipizide)
  - Meglitinides: nateglinide or repaglinide
  - Insulin: short acting (aspart, regular, and NPH)

- Switch to agents with lesser hypoglycemia potential if benefits > risks in continuing antihyperglycemic agents
  - Metformin, alpha-glucosidase inhibitors, DPP-4 inhibitors, GLP-1 agonists, SGLT2 inhibitors
  - Avoid TZDs due cardiac and stroke risks (pioglitazone)

Adjusting and stopping hypoglycemic agents

- Reduce doses or stop when renal function is impaired
  - Metformin: contraindicated in eGFR <30 mL/minute/1.73 m²
  - “Gliptins”: varying dose reductions for decreased renal function (eGFR 15-60 ml/minute/1.73 m²)
  - “Gliflozins”: contraindicated in eGFR <30 mL/minute/1.73 m²

- Evaluate for possible drug-drug interactions which can affect hypoglycemia agents or cause additive hypoglycemia
  - Quinolones, beta-blockers, trimethoprim/sulfamethoxazole, salicylates
When to taper: antihypertensives

• Optimal duration of treatment unknown
  • JNC 8 guidelines: Goal BP <140/90 based on risk factors/age
  • ACS and HF guidelines recommend indefinite use
  • ADA suggests less strict BP goal at end of life: <150/100

• Evaluate risk of hypotension and adverse events vs recurrence of disease or symptoms
  • Afib, heart failure symptoms, rebound hypertension/tachycardia, angina, AMI
How to taper: antihypertensives

• Beta blockers should not be abruptly stopped!!
  • Ventricular arrhythmias, severe angina, and myocardial infarction have been reported
  • Gradually taper over minimum of 1-2 weeks to decrease risk for rebound symptoms

• Clonidine also requires gradual taper over days to weeks
  • Abrupt withdrawal = rapid BP rise and sympathetic overload symptoms

• ACE Inhibitors/ARBs offer decreased risks of withdrawal or rebound symptoms = safer to discontinue without taper

When to taper: Proton pump inhibitors

- Long term use of PPIs is associated with increased risk of fracture, C. Diff infection, CAP, diarrhea, vitamin and electrolyte deficiencies.

- Stopping PPIs abruptly may cause rebound reflux symptoms.

- Not all patients are candidates for deprescribing:
  - Continue: Barrett’s esophagus, GI ulceration, severe esophagitis, chronic NSAID/steroid use.
  - Insufficient treatment duration: peptic ulcer, H.Pylori, GERD with mild-moderate esophagitis.

How to taper: Proton pump inhibitors

• Tapering approaches equally recommended
  • 50% dose daily vs alternate day dosing
  • Stop and use on-demand dosing
  • Twice daily to once daily frequency
    • Assess BID indication: H. Pylori or hypersecretory disease - do not deprescribe

• Use on-demand dosing if symptoms return after discontinuation
  • Resume at low daily dosing until resolution then stop again
  • Manage occasional symptoms with as needed OTC antacids

Cognitive Enhancers: Cholinesterase Inhibitors (CHEI) 
Aricept, Galantamine or Rivastigmine

• When:
  • Cognitive +/- functional decline over past 6 months
  • No noticeable benefit
  • Severe dementia (near total dependence for activities of daily living)

• How:
  • Reduce dose 25-50% every 1-2 weeks

• Withdrawal:
  • Reduced ability to concentrate, labile mood, hallucinations/delusions, agitation
Cognitive Enhancers: NMDA Receptor Antagonists

Memantine

- **When:**
  - Cognitive +/- functional decline over past 6 months or near total dependence
  - No noticeable benefit
  - If eGFR < 30: max daily dose of 5mg twice per day

- **How:** (limited/no RCT for guidance)
  - Immediate release: reduce by 5mg weekly
  - Extended release: reduce by 7mg weekly

- **Monitor:**
  - Cognitive dysfunction, behavioral changes, insomnia (?)
Does anyone have an answer about seizure prophylaxis???

- Prophylactic use of antiepileptic drug (AED) is not recommended in patients with intracranial hemorrhage
  - Subarachnoid hemorrhage controversial with limited trials

- Neurocritical Care Society and 2012 American Heart Association/American Stroke Association Guidelines
  - Short course is preferable (3-7) days if prophylaxis needed
  - Long term use if known risk factors:
    - Delayed seizure disorder (prior seizure), intracerebral hematoma, intractable HTN, CVA or aneurysm of MCA
But my patient has a brain cancer!

- American Academy of Neurology Practice Parameters
  - AED prophylaxis had no significant preventive effect on seizure incidence or seizure free survival in patients with brain neoplasms
  - AED prophylaxis associated with significant side effects:
    - Rash, nausea, vomiting, confusion

- Does this apply to brain metastasis?
  - Randomized control trials: no significant difference in seizure incidence
    - Similar findings with short 7 day course but increase in side effects

My patient had brain surgery!

- Current guidelines for post-op patients who have never had seizure
  - Discontinue or taper after first week post-op
  - Especially in those with medication side effects
Who has highest risk of seizures and may benefit from short course AED?

Table 6
Seizure prophylaxis protocol in neuro-ICU

<table>
<thead>
<tr>
<th>Seizure prophylaxis</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitive prophylaxis</td>
<td>• Severe TBI (7 days)</td>
</tr>
<tr>
<td>Probable prophylaxis</td>
<td>• Unsecured aneurysm in SAH</td>
</tr>
<tr>
<td></td>
<td>• Elevated intracranial pressure (ICP) and concern for poor compliance</td>
</tr>
<tr>
<td>Possible/no prophylaxis</td>
<td>• ICH</td>
</tr>
<tr>
<td></td>
<td>• AVM</td>
</tr>
<tr>
<td></td>
<td>• Cavernoma</td>
</tr>
<tr>
<td></td>
<td>• Brain neoplasm</td>
</tr>
<tr>
<td></td>
<td>• Malignant ischemic stroke</td>
</tr>
<tr>
<td></td>
<td>• Postoperative craniotomy</td>
</tr>
<tr>
<td></td>
<td>• Meningitis</td>
</tr>
<tr>
<td></td>
<td>• Cerebral venous sinus thrombosis (CVST)</td>
</tr>
<tr>
<td></td>
<td>• PRES</td>
</tr>
</tbody>
</table>
Who Gets to Stop Seizure Prophylaxis?

• If your patient has been on AED for >1 week
• Has side effects from medication
• Trouble with swallowing pills
• Have benzodiazepines on board just in case!!!
Consider Renal Dosing of Medications

- Gabapentin
- Pregabalin
- Venlafaxine
- Duloxetine
- Methadone
Gabapentin

• When:
  • eGFR >30-59 mL/minute/1.73 m²: 200-700 mg twice daily
  • eGFR >15-29 mL/minute/1.73 m²: 200-700 mg once daily
  • eGFR <15 mL/minute/1.73 m²: use with caution

• If discontinuing: taper gradually over ≥1 week

• Monitor:
  • Increased seizure frequency (in patients with epilepsy)
  • Confusion, irritability, tachycardia or diaphoresis
Pregabalin

**When:**

- eGFR 30-60 mL/minute/1.73 m²: reduce daily dose by 50% BID/TID
- eGFR 15-30 mL/minute/1.73 m²: reduce by 50-75% pending on start dose, single daily dose
- Caution with extended release and ESRD

- If discontinuing: taper gradually over ≥1 week

**Monitor:**

- Increased seizure frequency (in patients with epilepsy)
- Agitation, delirium, delusions, GI symptoms, mood changes or diaphoresis
Venlafaxine

• When:
  • Mild to severe renal impairment: reduce dose by 25-50%
  • Mild to severe hepatic impairment: reduce dose by 50%

• If discontinuing: taper gradually over 2-4 weeks

• Monitor:
  • Re-emerging original symptoms
Duloxetine

• When:
  • eGFR <30 mL/minute/1.73 m² and ESRD: avoid use
  • Hepatic impairment: avoid use

• If discontinuing: taper gradually over 2-4 weeks

• Monitor:
  • Re-emerging original symptoms
Methadone

• When:
  • eGFR <10 mL/minute/1.73 m²: Administer 50% to 75% of normal dose
  • Hemodialysis or peritoneal dialysis does not increase elimination of methadone
  • On other QTc prolonging or cytochrome p450 medications

• If discontinuing: taper gradually over weeks

• Monitor:
  • Opioid withdrawal - GI upset, sweating, yawning, goose bumps
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  - Aspirin 81 mg daily
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Online Resources

- AGS Beers Criteria resources
  - Alternative Medications List
  - Criteria and evidence table
- Deprescribing.org Guidelines and Algorithms
- Canadian Deprescribing Network (CaDeN)
  - Patient resources and brochures
- Polypharmacy Guidance, NHS of Scotland
- OncPal Deprescribing Guideline
KEEP CALM
it's QUESTION TIME
References

- American Heart Association Stroke Council; Council on Cardiovascular Nursing; Council on Peripheral Vascular Disease; Council on Clinical Cardiology Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013
References


- Reeve E, To J, Hendriksen, Shakib S, Roberts MS, Wiese MD. Patient barriers to and enablers of deprescribing: a systematic review. Drugs Aging 2013; 30: 793-807


