When is it too many?
The art and science of deprescribing

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Disclosure

I have no conflict of interest to report.
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INTRODUCTION

CASE PRESENTATIONS
Mrs. Elder

96 year old, living alone at home. Independent for ADLs. Cooks simple meals. Daughters help for other IADLs. Walks independently but sedentary.

PMHx: OA, Glaucoma, Remote Cholecystectomy

Rx: Acetaminophen PRN, betoptic 1 drop O.U. BID
Mrs. Elder
Outpatient routine visit

B.P. 180/95 both arms
BMI 28
Otherwise, normal exam.

Random glucose 14.1
ECG: Sinusal, LVH signs
Mrs. Long

93 year old, admitted to a CHSLD
End-stage CKD (eGFR 10)
Remote lacunar stroke
Dementia (FAST 7a) and BPSD: long periods of somnolence alternating with outbursts of verbal and physical aggressiveness
Frequent falls Severe weight loss (BMI 19)
COPD, HTN, Hypothyroidism, GERD, Macular degeneration, Anxiety/Depression, CAD, Osteoporosis (ribs #- T-spine vertebral #)
List of Rx when admitted to LTC

- Acetaminophen 1g TID
- Clopidogrel 75mg die
- Levothyroxine 125mcg die
- Montelukast 10mg die
- Fluticasone/Salmeterol 250-50 mcg 1 inh. q 12h
- Memantine 10mg BID
- Alprazolam 0.25 mg BID and TID PRN
- Mirtazapine 15mg HS
- Zolpidem CR 6.25 mg HS

- Amlodipine 10mg die
- Famotidine 20mg BID
- Metoprolol 25mg BID
- Donepezil 10mg die
Mrs. Best

79 year old, married, living at home with husband
Independent for ADLs and IADLs. Active.

COPD, DMII, HTN, Osteoporosis, OA
At what age should we stop or withhold medications?

Better then the age criteria:

**AMA criteria**: Chances of success, QOL, Duration of benefits, Urgency, the quantity of resources required

**Patient-centered approach**: information-sharing and discussion, goal-oriented and proportionate care.
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TREATMENT OF HYPERTENSION IN THE FRAIL ELDERLY
Hypertension in patients >80

B.P. increases with age and 80 % of individuals >80 years old in North-America have systolic HTN. Increased pulse pressure= increased arterial stiffness.
Greater BP variability.
Increased prevalence of orthostatic and post-prandial hypotension.
Decreased capacity to the kidney to adjust to volume and sodium changes.
BP and risk of mortality and morbidity in the old old

From observational studies:
Cardiovascular M & M increases with BP- even in the elderly BUT the association is lost vs inverted in the frail old.

Prospective Study Collaboration vs National Health and Nutrition Examination Survey
Diastolic BP J-curves with diastolic BP<70mmHg is associated with increased mortality
Low diastolic BP vs increased BP?
Orthostatic hypotension increases vascular mortality but this association may be present only in the frail old.
Risk of functional disabilities

HTN during midlife increases the risk for cognitive impairment and physical impairment later in life (60% increased risk of dementia).

In old old, lower BP is associated with more rapid physical and cognitive decline and more severe dementia.

The association is not well understood in the old old (low BP as a cause of decline vs marker of underlying comorbidities).
Anti-hypertensives in the old old

Guidelines suggest tx of HTN in individuals >80 year-old based on trials (including HYVET) and Meta-A (<7000 patients).

Caution:
- Inclusion of pts with HTN >160 mmHg
- No evidence for benefits <140 mmHg
- Generalizability of studies controversial

Some evidence of increased mortality if BP is decreased by more then 15-20mmHg and/or >2 drugs are used
Anti-hypertensives in the old old

Recommendations:
Target systolic BP: 140-160
Diastolic BP $\geq$ 65-70
Maximum 2 or 3 drugs
Target reduction $< 15-20$ mmHg
Diuretics and calcium channel blockers may be preferable in isolated systolic HTN
In frail pts, decision to treat must be individualized and depends on treatment tolerability
?Do not start a Rx in patient $> 80$, unless BP $> 180$
Review anti-hypertensives treatment in the old old

In older/frail patients on >2 drugs and BP<140mmHg, consider decreasing anti-hypertensives to decrease risks of polypharmacy. Consider decreasing/stopping Rx if diastolic BP <70, orthostatic hypotension, polypharmacy, increasing frailty.

Risks include recurrence of HTN and fluid overload(with diuretics).
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OSTEOPOROSIS PROPHYLAXIS
Osteoporosis: a condition of the old

Guidelines do not address specifically the frail or the old old.

Studies indicate under risk identification and treatment of older population at high risk.

Given the morbidity/QOL loss associated with fractures, more efforts is necessary to identify risks and treat.
Osteoporosis: current treatment and upcoming alternatives

No protective effects of bisphosphonates on hip or wrist fractures have been noted in women aged more than 80 years with no prior hip or vertebral fractures. Oral bisphosphonates may represent a challenge in frailer patients. **IV bisphosphonates once a year are increasingly available, maybe better tolerated, show more rapid results but are contra-indicated in severe RF. It is often difficult to obtain reimbursement.**

Bisphosphonates lose their benefits over time and can increase risks. **Need to be stopped after 5 years** of tx.

Newer alternatives may become available (Strontium ranelate, Denosumab, teriparatide, cathepsin K inhibitor).
Osteoporosis prophylaxis in NH

• Calcium and Vitamine D supplementation are recommended in NH patients.
• Osteoporosis prophylaxis should be reassessed in bed-bound patient at low risk of falls.
Recommended readings

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DMII MANAGEMENT IN THE FRAIL ELDERLY
Glycemic targets should be individualized taking into account functional status, comorbidities, especially the presence of established CVD, history and risk of hypoglycemia, and presence of microvascular complications. (International Diabetes Federation)

<table>
<thead>
<tr>
<th>Functional category</th>
<th>HbA1C target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independent</td>
<td>7-7.5%</td>
</tr>
<tr>
<td>Dependent</td>
<td>7-8%</td>
</tr>
<tr>
<td>Frail</td>
<td>Up to 8.5%</td>
</tr>
<tr>
<td>Dementia</td>
<td>Up to 8.5%</td>
</tr>
<tr>
<td>End of Life</td>
<td>Avoid symptomatic hyperglycemia</td>
</tr>
</tbody>
</table>
Recommended readings

International Diabetes Federation, Managing Older People with Type 2 Diabetes. Global guideline. IDF 2013, www.idf.org
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COPD TREATMENT IN THE ELDERLY
Treatment of COPD in the elderly

Inhaled therapies are the cornerstone of treatment but devices prove difficult to use and the regimen are often complex.

Recent evidence suggests that goals of reducing symptoms and risks and allowing for an optimal QOL are largely unmet in elderly patients in NH.

In one study, 50% of pts with MCI and 100% of pts with mild dementia could not operate the metered doses inhalers (MDI). Decreased hand strength affect the capacity to use appropriately the MDI.
Treatment of COPD in the elderly

Worsening hypoxia or hypercapnia can worsen cognitive function.

COPD patients have multiple comorbidities (average of 9), contributing to increased dyspnea.
Recommended readings

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TREATMENT OF DEMENTIA
Are medication effective in treating the cognitive symptoms of Alzheimer’s?

There are no medications that have been demonstrated to alter the underlying disease process associated with AD.

Statistically significant but **clinically modest** improvements in cognitive symptoms of mild-to-moderate AD have been observed with donepezil, galantamine and rivastigmine. All **cholinesterase inhibitors** also produce modest benefits on global clinical ratings and ADLs.

**Adverse events** (dose related) include nausea, vomiting and diarrhea. Also bradyarrhythmias and syncope-related outcomes.

**Memantine** is associated with statistically significant but clinically modest effects in global, cognitive and functional improvements in patients with moderate-to-severe AD. According to a Cochrane review, patients taking memantine are less likely to develop agitation. Memantine is well tolerated.

**Patients with multiples comorbidities are excluded from studies.**
Recommended readings


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BMI 28
Otherwise, normal exam.

Random glucose 14.1
ECG: Sinusal, LVH signs
**Useful to know** (actuarial data- Globe and Mail, April 15, 2014)

<table>
<thead>
<tr>
<th>Men (age)</th>
<th># years remaining</th>
<th>Women</th>
<th># years remaining</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>9.5</td>
<td>80</td>
<td>11.2</td>
</tr>
<tr>
<td>85</td>
<td>6.8</td>
<td>85</td>
<td>8</td>
</tr>
<tr>
<td>90</td>
<td>4.7</td>
<td>90</td>
<td>5.5</td>
</tr>
<tr>
<td>100</td>
<td>2.4</td>
<td>100</td>
<td>2.6</td>
</tr>
</tbody>
</table>
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Following recommended guidelines, what would be the drug regimen recommended?
According to the aggregate recommendations from the clinical practice guidelines:

**THE PATIENT WOULD BE PRESCRIBED 12 DRUGS IN 19 DOSES 5 TIMES PER DAY.**

**BOYD ET AL. JAMA 2005, VOL.294, NO 6, 716-724**
How applicable are Clinical Practice Guidelines to elderly patient with comorbidities?

Mutasingwa et al, Can. Fam. Physician 2011; 57:e253-262

Out of the 10 CPGs reviewed, 7 mentioned treatment of the elderly, 8 mentioned treatment with comorbidities, 4 indicated the time needed to treat to benefit in the context of life expectancy, 5 discussed barriers to implementation, and 7 discussed the quality of evidence.
Prognostication: Scott A Murray, Making a Difference with BMJ Group/University of Edinburgh
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Frequent falls
Severe weight loss (BMI 19)
COPD, HTN, Hypothyroidism, GERD, Macular degeneration, Anxiety/Depression, CAD, Osteoporosis (ribs # - T-spine vertebral #)

List of Rx when admitted to LTC

First review

Acetaminophen 1g TID
Clopidogrel 75mg die
Levothyroxine 125mcg die
Montelukast 10mg die
Fluticasone/Salmeterol 250-50 mcg 1 inh. q 12h
Memantine 10mg BID stopped
Alprazolam 0.25 mg BID and TID PRN
Mirtazapine 15mg HS
Zolpidem CR 6.25 mg HS stopped

Amlodipine 10mg die
Famotidine 20mg BID
Metoprolol 25mg BID
Donepezil 10mg die stopped
<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>1g TID</td>
<td></td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>75mg die</td>
<td></td>
</tr>
<tr>
<td>Levothyroxine</td>
<td>125mcg die</td>
<td></td>
</tr>
<tr>
<td>Montelukast</td>
<td>10mg die</td>
<td>Stopped</td>
</tr>
<tr>
<td>Fluticasone/Salmeterol</td>
<td>250-50 mcg 1 inh. q 12h</td>
<td>Stopped</td>
</tr>
<tr>
<td>Memantine</td>
<td>10mg BID</td>
<td></td>
</tr>
<tr>
<td>Alprazolam</td>
<td>0.25 mg BID and TID PRN</td>
<td>Changed to BID PRN(only used once every 2 weeks)</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>↓ 7.5 mg die</td>
<td></td>
</tr>
<tr>
<td>Zolpidem CR</td>
<td>6.25 mg HS</td>
<td></td>
</tr>
</tbody>
</table>

Changes made:
- Amlodipine: 10mg die
- Famotidine: ↓ 10mg die
- Metoprolol: 25mg BID
- Donepezil: 10mg die
- Mirtazapine: ↓ 7.5 mg die
Polypharmacy and Medicine-Related Harm

• The number of medicines a patient is taking is the single most important predictor of medicine related-harm.
• The estimated risk of ADE is 82% for 7 drugs or more.
• The more medicines, the greater risk of adverse drug reaction, drug-drug interaction, drug-disease interaction, cascade prescribing, nonadherence and drug errors.
• According to observational studies, >5 drugs increase the risk of frailty, falling and hospital admission.

JCOM 2016; 23 (8): 359-69
Deprescribing is the systematic process of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient’s care goals. Deprescribing should be seen as part of the good prescribing continuum, which spans medicine initiation, titrating, changing, or adding medicines, and switching or ceasing medicines.

Deprescribing is not about denying effective treatment to eligible patients. It is a positive, patient-centered intervention, with uncertainties, and requires shared decision-making, informed patient consent and close monitoring of effects.
Review of drug withdrawal trials
JAMA Internal Medicine 2015; 175 (5): 827-834

• Systematic review of 31 trials (15 randomized and 16 observational) of specific class of drugs, in 65 y.o. and over showed: **Safe** to discontinue in 80-100% antihypertensives, psychotropic drugs and benzodiazepines in selected individuals, with educational intervention and careful monitoring.
Polypharmacy reduction trials

The evidence for direct deprescribing is limited: few good studies, small patient samples, short-duration of follow-up, selection of clinical outcomes.

Deprescribing patient-specific interventions have been shown to reduce mortality significantly in older individuals (especially >80) in RC studies. Educational programs demonstrated no change in mortality.

Br J Clin Pharmacol 2016; 82: 583-623
Opportunities to review a patient’s drug regimen
Hogan D., *When to stop medications in the care of older patients* www.cpsa.ca, posted July 2014

When there is a change in the goals of care
At the time of consultations
During care transitions
When annual/semi-annual medication reviews are done
Whenever a patient presents with a new problem or complaint (always consider whether this could be an adverse drug effect)
Before prescribing a new medication
1. Ascertain current drug use: a “brown paper bag” review.

2. Identify patients at high risk of or experiencing adverse drug reactions: 8 or more drugs is one of the most predictive risk factors.

3. Estimate life expectancy in high risk patients: physicians are better at estimating prognosis than accurately identifying diagnoses(Geri-EM.com)

4. Define overall care goals with reference to estimated life expectancy: Integrate current level of irreversible disability, QOL, personal life priorities.
5. Define and confirm current indications for ongoing treatment: identify diseases-treatment mismatches (overuse, underuse, misuse)

6. Determine the time until benefit of disease-specific medication: relevant for medications aimed at primary and secondary prevention.

7. Determine disease-specific benefit-risk thresholds that may support treatment discontinuation: tools for calculating the absolute risk of disease or treatment-related events may provide values more precise than intuitive estimates.
8. Review the relative utility of individual drugs in older patients: likely clinical benefit, potential for harm and burden of administration and ongoing monitoring of drug effects.

9. Identify drugs that may be discontinued or reduced in dose.

10. Monitoring and reviewing treatment decisions.
Questions that can be used to initiate deprescribing

• Are treatment targets and care goals achieved by a specific drug?

• Is there an ongoing indication that justifies continuous use of a specific drug based on evidence of effectiveness?

• Does a non-drug therapy exist that may substitute for > or= 1 drug?

• Can we find a drug with a low benefit-risk ratio?
Questions that can be used to initiate deprescribing (2)

• Is a drug consistently associated with non-adherence as a result of side effects or lack of effect, burden of cost or inconvenience, or complexity of dosing schedules?

• Is there another drug that may be superior to the one in question for the same indication?

• Are there duplications in drug therapy (i.e. 2 drugs from the same class)?
Questions that can be used to initiate deprescribing (3)

• Is a combination drug used in which one of the component is inappropriate?
• Is a drug being used that carries a risk of addiction or accumulation over the medium or long-term?
• Are there lower effective doses for specific drugs, particularly in the presence of more conservative treatment targets?

AJM 2012; 125:529-537
Questions that can be used to initiate deprescribing (4)

• Are 1 drug or more being prescribed to counter side effects or ADR of another drug? If so, can the drug that caused the ADR be withdrawn or substituted with another less troublesome agent?

• Can a drug be withdrawn or have its dose reduced with no significant risk?

AJM 2012; 125:529-537
Other tools to identify drugs for discontinuation

• The 2012 Beers Criteria JAGS
• AGS/Choosing wisely: Five things physicians and Patients should Question. Part 1 and 2.
• START (Screening Tool to Alert doctors to Right i.e appropriate, indicated treatment): Gallagher et al. Age Ageing 2007; 36:628-631
• Good Palliative-Geriatric Practice Algorithm: Garfinkel D, Mangin D, Arch Intern Med 2010; 170:1648-54
Recommended readings


Recommended readings (2)

Scott et al. **Minimizing Inappropriate Medications in Older Populations: A 10-step Conceptual Framework**
AJM 2012; 125:529-537

Scott et al. **Reducing Inappropriate Polypharmacy: The Process of Deprescribing**
JAMA Internal Medicine 2015; 175 (5): 827-834

Scott et al. **Evidenced-based Deprescribing: Reversing the Tide of Potentially Inappropriate Polypharmacy**
JCOM 2016; 23 (8): 359-369
Thank You!

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