Polypharmacy & De-prescribing In Older Adults
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The Geriatric 5Ms

Mobility
Mind
Medications
Multimorbidity
Matters Most
HOW MANY MEDICATIONS DOES IT TAKE TO GET TO POLYPHARMACY?

"The red are for the illness, the blue are for the side effects of the red and the green are for the effects of the blue."
OBJECTIVES

1. Identify when a patient has problematic pharmacy

2. Select and use an appropriate tool to determine a de-prescribing plan

3. Create a short-term and long-term plan to optimize patients medication safety
Who here has a patient with polypharmacy?

How do you know your patient has polypharmacy?

What do you think led the patient to have polypharmacy?

What are the consequences of polypharmacy?

What are the barriers to de-prescribing?

Have you attempted to do anything about the polypharmacy?
• The problem **effects many**¹

• The problem **is growing**²

• The problem **has a negative impact**³

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By age 70:

75% of patients take ≥ 5 medications

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Number of people > 65 years old taking ≥ 5...

<table>
<thead>
<tr>
<th>Year</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>12.80</td>
</tr>
<tr>
<td>2010</td>
<td>39.00</td>
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Increased rates of drug interactions, impaired cognition, frailty, falls, morbidity and disability
The rising tide of polypharmacy and drug-drug interactions: population database analysis 1995–2010

Bruce Guthrie¹, Boikanyo Makubate², Virginia Hernandez-Santiago¹ and Tobias Dreischulte³

WHAT MAKES MEDICATION USE SO CHALLENGING IN THE OLDER ADULT?

- Low representation in research
- Health system factors that compound complexity
- Physiologic changes (PK/PD)
Review of Pharmacokinetic Changes

Pharmacokinetics – How the body reacts to the drug

- **Absorption**
  - Increased gastric pH
  - Reduced gastric motility, secretions and blood blow

- **Distribution**
  - Decreased body water
  - Increased body fat
  - Decreased protein binding

- **Metabolism**
  - Decreased hepatic blood flow
  - Decreased liver mass/size

- **Elimination**
  - Reduced glomerular filtration rate
  - Reduced muscle mass (↓ Scr)

Lipophilic

Hydrophilic
Review of Pharmacodynamic Changes

Pharmacodynamics—How the drug reacts to the body

Changes in:
- Receptor Binding
- Post receptor effects
- Homeostatic responses
- Blood brain barrier permeability

Effects of drugs at similar concentrations
- Analgesics
- Anticholinergics
- Anticoagulants
- Benzodiazepines
- Beta blockers

WHY HAVEN'T WE CURED POLYPHARMACY?
Challenges and Enablers of Deprescribing: A General Practitioner Perspective

“Why don’t we deprescribe? Is that a knowledge issue? Possibly. It’s very complicated. Do we know all the interactions and side effects of all these drugs? Of course we don’t.” GP4

“But you don’t have guidelines a lot in the elderly, do you? That’s the hardest thing.” GP10

“It’s because, obviously you’ve got a clinical responsibility. Stopping a medicine is in a way no less a therapeutic position than starting a medicine. So you’ve still got to then consider the down flow effects of that on the patient, so you need a management plan.” GP4

“I do think sometimes, you wonder who are we treating? Are we treating the nursing staff who can’t face somebody calling out at night, or are we treating actual patient who may be very well, happen to be calling out once or twice a night at one o’clock, but then fall back to sleep, you know?” GP9

“I don’t have that much time... for those kind of moral routine stuff, because I already have a lot of acute stuff I got to deal with on the days that I go there.” GP9

Fig 1. Deprescribing considerations and challenges.
Deprescribing

- Planned and supervised process of dose reduction or stopping of medication(s) that may be causing harm or are no longer providing benefit

Is It Safe to De-prescribe?

- Good Palliative-Geriatric Practice algorithm to 70 community dwelling older adults to recommend drug discontinuation
- Mean age 82.8 years
- 61% had 3 or more comorbidities, 26% had 5 or more
- They recommended discontinuation of 58% of drugs (!), only 2% of which were restarted

Garfinkel, D, Mangin, D. Feasibility Study of a Systematic Approach for Discontinuation of Multiple Medications in Older Adults. Arch Intern Med. 2010;170(18):1648-1655.14
Is It Safe to De-prescribe?

YES!

“Discontinuation of a mean (range) 4.2 (1-11) different medications in the cohort was safely achieved with no significant adverse events or deaths related to discontinuation. Only 2% of drugs had to be readministered; in 88% of elderly patients, application of the GP-GP algorithm was associated with subjective clinical, functional, mood, or cognitive improvement.”

GarfinkelD, ManginD. Feasibility Study of a Systematic Approach for Discontinuation of Multiple Medications in Older Adults. Arch Intern Med. 2010;170(18):1648-1655.15
Deprescribing Protocol

1. Reconcile all medications according to indication
2. Appropriateness; Consider Risks/benefits of medications
3. Assess each drug for eligibility to be discontinued
4. Prioritize drugs for discontinuation
5. Implement and monitor drug discontinuation

Scott IA et al. JAMA. 2015; 175(5):827-834.
1. Reconcile all medications according to indication

1. Reconcile all medications according to indication

What is the patient actually taking?

Does this medication have an indication?

Case Example:
Mr. RX is an 87 year old male

Medications:
1. Amlodipine 10 mg daily
2. Alprazolam 1 mg twice daily
3. Atorvastatin 80 mg daily
4. Glyburide 10 mg twice daily
5. Metformin 500 mg daily
6. Lisinopril 40 mg daily
7. Omeprazole 20 mg daily
2. Appropriateness; Consider Risks/benefits of medications

Use Medication Assessment Tools!

Try the Deprescribing Protocol in your Patient

1. Reconcile all medications according to indication
2. Appropriateness; Consider Risks/benefits of medications
3. Assess each drug for eligibility to be discontinued
4. Prioritize drugs for discontinuation
5. Implement and monitor drug discontinuation

Mr. RX is an 87 year old male
DM, HTN, Mild anxiety
BP ranges 130s/70s.
His blood sugars – he checks twice a week
Range 82 – 230
HgbA1c 7.2.

**Medications:**
1. Amlodipine 10 mg daily
2. Alprazolam 1 mg twice daily
3. Atorvastatin 80 mg daily
4. Glyburide 10 mg twice daily
5. Metformin 500 mg daily
6. Lisinopril 40 mg daily
7. Omeprazole 20 mg daily
Case Example 1

Mr. RX is an 87 year old male

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6. Lisinopril 40 mg daily
7. Omeprazole 20 mg daily

- HTN
- anxiety
- HLD
- DM
Case Example 1

Mr. RX is an 87 year old male

Medications:
1. Amlodipine 10 mg daily
2. Alprazolam 1 mg twice daily
3. Atorvastatin 80 mg daily
4. Glyburide 10 mg twice daily
5. Metformin 500 mg daily
6. Lisinopril 40 mg daily
7. Omeprazole 20 mg daily

Options:
- HTN
- anxiety
- HLD
- DM
Eligibility
- Potential or Active ADR
- No indication
- Ineffective
- Prescribing cascade
- Treatment burden
- Safer alternatives
- Goals of care
  - Blood pressure
  - A1c
4. Prioritize drugs for discontinuation

- **Priority**
  1. Greatest harm and least benefit
  2. Easiest to discontinue, lowest likelihood of withdrawal
  3. Patient is willing to discontinue (“buy-in”)

- **Anticipated barriers**
  - Rebound symptoms
    - (acid-suppressive therapy)
  - Withdrawal symptoms
    - (antidepressants, benzo’s opioids)
  - Patient attachment
  - Patient/provider relationship
Elimination depends on half-life ($t \frac{1}{2}$)
- $5 \times t \frac{1}{2} = 98\%$ eliminated

Elimination depends on mechanism
- Reversible/temporary inhibition: $t \frac{1}{2}$
- Irreversible or production/expression change: depends on lifespan of receptor/cell (EX: SSRI 4-6 weeks, PPI 72 hours)

- Drug concentration
- Drug effect

• Plan discontinuation strategy:
  – Drug concentration (A)
  – Decrease dose (B)
    • Less peak/trough fluctuation
      – EX: 1 mg twice daily → 0.5 mg twice daily
  – Extend dose interval (C)
    • More peak/trough fluctuation
      – EX: 1 mg twice daily → 1 mg once daily
  – Extended Release formulation (not pictured)
    • Increase half life and less fluctuation
      – EX: 1 mg IR twice daily → 1 mg ER once daily

http://medstopper.com/
5. Implement and monitor drug discontinuation

- Written instructions
- Patient involvement
- Follow-up scheduled
- Plan a back up or threshold to restart
- Monitor for Adverse Drug Withdrawal Event (ADWE)
  - Physical withdrawal (tachycardia, rebound GERD)
  - Symptoms of underlying condition (disease reemergence)
  - Risk increases with prolonged use, higher doses, shorter half life

**Stopping medications should be done with the same considerations as starting**
Case Example

Mr. RX is an 87 year old male

Medications:
1. Take alprazolam 0.5 mg qAM and 1 mg qPM x 1 week, then take 0.5 mg twice daily x 1 week, then take 0.5 mg at bedtime only x 1 week, then take 0.25 mg at bedtime PRN. Report increased anxiety, shakiness, or difficulty sleeping
2. Take omeprazole every other day x 1 week, then stop. Report increased heartburn or acid reflux symptoms. May try tums PRN.
Mrs. MR is an 84 yo F with Alzheimer’s dementia, HTN, osteoporosis, CKD, anemia, urinary incontinence, hyperlipidemia. Frail, 90 lbs (BMI 17), BP 95/60, declining health.

**Medications:**
1. Donepezil 10 mg po daily
2. Lovastatin 40mg po qHS
3. Magnesium oxide 400mg po daily
4. Metoprolol tartrate 50mg po BID
5. Quetiapine 25mg po q AM
6. Sertraline 12.5mg po q AM
7. Hydrochlorothiazide 12.5mg po daily
8. Losartan 100mg po daily
9. Omeprazole 20mg po daily
Case Example:
Mrs. MR is an 84 yo F

**Medications:**

1. Donepezil 10 mg po daily
2. Lovastatin 40mg po qHS
3. Magnesium oxide 400mg po daily ?
4. Metoprolol tartrate 50mg po BID
5. Quetiapine 25mg po q AM
6. Sertraline 12.5mg po q AM
7. Hydrochlorothiazide 12.5mg po daily
8. Losartan 100mg po daily
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Case Example:
Mrs. MR is an 84 yo F

Medications:
1. Donepezil 10 mg po daily
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3. Magnesium oxide 400mg po daily?
4. Metoprolol tartrate 50mg po BID
5. Quetiapine 25mg po q AM
6. Sertraline 12.5mg po q AM
7. Hydrochlorothiazide 12.5mg po daily
8. Losartan 100mg po daily
9. Omeprazole 20mg po daily?
Case Example:

Mrs. MR is an 89 yo F

**Medications:**

1. Discontinue magnesium.
2. Discontinue hydrochlorothiazide, record home blood pressure readings.
3. Take omeprazole every other day x 1 week, then stop. Report increased heartburn or acid reflux symptoms. May try tums PRN.
4. Stop taking statin.
5. Reconsider sertraline.
6. Follow-up on Quetiapine and need to re-dose at every visit.
Try the Deprescribing Protocol in your Patient

1. Reconcile all medications according to indication
2. Appropriateness; Consider Risks/benefits of medications
3. Assess each drug for eligibility to be discontinued
4. Prioritize drugs for discontinuation
5. Implement and monitor drug discontinuation

Scott IA et al. JAMA. 2015; 175(5):827-834.
Take Home Points

1. Less is more
2. Use tools to identify inappropriate medications
3. Have a specific plan for how the patient should discontinue their medication, monitoring and follow-up plan
4. Involve your patients
### Design

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients admitted to community hospital (n = 275) ≥ 65 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Medication profiles analyzed via multi-drug cytochrome-specific software</td>
</tr>
<tr>
<td>Results</td>
<td>CYP-mediated DDI’s detected among 80% of patients For each medication added to a 5-drug regimen, the probability of potential CYP-mediated DDIs increased by 12% (OR 1.12; 95% CI 1.09-1.14)</td>
</tr>
</tbody>
</table>

**Graph:**

- **Number of medications:** 5 to 9, 10 to 14, 15 to 19, 20 or more
- **Probability of DDI’s:** 0, 20, 40, 60, 80, 100

**Bar Chart:**

- 5 to 9: 50
- 10 to 14: 81
- 15 to 19: 92
- 20 or more: 100

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POLYPHARMACY → ADVERSE OUTCOMES

The number of concomitant medications associated with outcomes and mortality

<table>
<thead>
<tr>
<th>Frailty</th>
<th>≥ 6.5 medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disability</td>
<td>≥ 5.5 medications</td>
</tr>
<tr>
<td>Mortality and incident falls</td>
<td>≥ 4.5 medications</td>
</tr>
</tbody>
</table>

POLYPHARMACY → FALLS

Medication use and risk of falls among nursing home residents: a retrospective cohort study

- Polypharmacy (> 4 medications) was a significant risk factor for falls (98.2% vs 85.9%; p = 0.010)
- Pantoprazole was a significant risk factor for falls
  - PPV (95% CI) = 0.40 (0.3-0.52)
  - NNH = 6

Bor A et al. Int J Clin Pharm 2017
POLYPHARMACY ➔ IMPAIRED GAIT AND COGNITION

### TABLE 2 | Results of the logistic regression analysis.

<table>
<thead>
<tr>
<th>Multivariate logistic regression</th>
<th>Number of molecules ≤5 vs. &lt;5</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>MoCA (&lt;26) vs. MoCA (≥26)</td>
<td>3.153</td>
<td>1.187 – 8.373</td>
</tr>
<tr>
<td>TUG (-) vs. TUG (+)</td>
<td>2.753</td>
<td>1.046 – 7.249</td>
</tr>
<tr>
<td>Number of comorbidities (&lt;2 vs. ≥2)</td>
<td>8.730</td>
<td>3.000 – 25.404</td>
</tr>
</tbody>
</table>

*MoCA, Montreal Cognitive Assessment; TUG, Timed Up and Go.*
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Special thanks to Drs. Andrea Schwartz, Sarah Berry, and Laura Triantafylidis, PharmD!