De-prescribing Medications: First Do No Harm

ACP Illinois Chapter
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Pertinent disclosures

• No financial relationship with any drug manufacturer
Objectives

• Examine the issue of polypharmacy
• Discuss opportunities to decrease adverse drug events
• Introduce the concept of de-prescribing
• Describe the potential benefits & risks of de-prescribing
• Explain how providers and patients can de-prescribe medications
Polypharmacy

• Simultaneous use of multiple drugs to treat one or more medical conditions (often implies some are not medically necessary)

• COMMON:

Prevalence increases w/ age; in developed countries, 30% of elderly are prescribed 5 or more drugs *

Qato DM, et al. JAMA 2008;300(24)
1. Metformin 500 mg x 86.5 mg 3 times daily
2. Metformin 1 capsule
Polypharmacy: particularly common in elderly

- 20% of drugs used in the elderly may be inappropriate (1)
- 1/3 of drugs used in nursing homes may be inappropriate (2)
- 20-60% of elderly are taking at least 1 potentially inappropriate drug (3)

Polypharmacy: Don’t forget CAM

- 42% of patients fail to inform their providers about use of complementary & alternative medications
- Why?
  
  My doctor didn’t ask
  I didn’t think my doctor needed to know

Polypharmacy: Don’t forget OTCs

- 40% of OTCs purchased by elderly
- Use of OTCs is 3-fold higher in elderly

Polypharmacy

• COMMON
  in developed countries, 30% of elderly are prescribed 5 or more drugs*

• RISKY
  adverse drug events (ADEs)

Qato DM, et al. JAMA 2008;300(24)
Adverse drug events

• Associated with
  incr risk of hospital admission (1)
  incr length of hospital stay (2)
  incr risk of inpt death (2)
  incr risk of hospital re-admission (3)

HOSPITALIST CLOSED CLAIMS STUDY

An Expert Analysis of Medical Malpractice Allegations

Darrell Ranum, JD, CPHRM, Vice President, Department of Patient Safety and Risk Management
David B. Troxel, MD, Medical Director
Robin Diamond, MSN, JD, RN, Senior Vice President, Department of Patient Safety and Risk Management

STUDY DESIGN

We analyzed 464 claims* against hospitalists that closed from 2007–2014. The study, based on the claims experience of more than 2,100 hospitalists insured by The Doctors Company, includes all claims and lawsuits (cases) in which a hospitalist was named as a defendant.
HOSPITALIST CLAIMS BY ALLEGATION 2007–2014

- Diagnosis related (failure, delay, wrong): 36%
- Improper management of treatment: 31%
- Medication-related error: 11%
- Improper performance or delay in treatment or procedure: 5%
- Failure to treat: 3%
- Failure to monitor physiologic status: 3%
Inappropriate use of drugs

• “The number of drugs that a patient is taking is the single most important predictor of harm” (1, 2)

• “This high level of iatrogenic harm mandates a response from prescribing clinicians.” (2)

Polypharmacy Drivers

• Clinical guidelines, coupled w/ guideline derived quality indicators & performance incentives*
• Patient expectations*
• Adverse drug effects being misinterpreted as new problems requiring more drugs*
• Access to medications? Medicare Part D

Steps to prescribe a drug

- Define the pt’s problem
- Specify the therapeutic objective
- Select the most appropriate drug therapy
- Provide info, instructions & warnings
- Routinely evaluate the pt for side effects
- What’s often missing?
- Setting expectations & goals on when to stop therapy
Strategies to address potentially inappropriate medications (PIMs)

- Comprehensive medication reviews
- Educational interventions
- Prescribing audits w/ feedback

Reeve E, et al. Drugs Aging 2013; 30
De-prescribing

• “The systematic process of identifying and discontinuing drugs in instances in which existing or potential harm 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 et al. JAMA IM May 2015 Vol 175; No 5
Why de-prescribe? improve outcomes

• Review: withdrawal of psychotropics & benzodiazepines are associated with:
  reduction in falls
  improvement in cognitive and psychomotor function

Van der Cammen, et al. Age Ageing 2014;43(1)
Is it safe to de-prescribe?

- A systematic review of 31 drug withdrawal trials (15 randomized, 16 observation) of specific drug classes in the elderly demon that drugs can be d/c’ed without harm in 20% to 100% of pts (1)

  Anti-hypertensives
  Psychotropics
  Benzodiazepines

Is it safe to de-prescribe? antipsychotics

• Review of 9 randomized trials: In > 80% of pts w/ dementia, safe to withdraw antipsychotics which had been used continuously for behavioral and psychological symptoms

Is it safe to de-prescribe? benzodiazepines

- Randomized trial: pt education from community pharmacists led to 77% reduction in benzodiazepine use among long-term users at 6 mos w/out withdrawal seizures of other ill effects.

Keys to safe De-prescribing

• Appropriate patient selection
• Patient education
• Careful withdrawal
• Close monitoring
Why doctors don’t de-prescribe?

• Lack of awareness
• Clinical inertia
• They perceive themselves as being ill-equipped
• Belief de-prescribing is not feasible

De-prescribing Tools

• American Geriatrics Society Beers Criteria

• STOPP / START Criteria
STOPP/START Criteria

• Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START)

- as intervention applied w/in 72 hrs of hosp admission, sig reduced ADEs & LOS by 3 days*

1. Furosemide 80 mg, 1 a day, stop set.
2. Atorvastatin 20 mg.
3. Warfarin 5 mg.
4. Omeprazole 20 mg, 1 a day, 20 mg.
5. Allopurinol 300 mg.
6. Metformin 500 mg, 1 a day, 500 mg, x2.
7. Metoprolol Table x4, 100 mg.
8. Lisinopril 50 mg.
9. Aspirin 325 mg.
10. Folic acid 1 mg.
11. Tamsulosin 4 mg.
De-prescribing principles

• Pt-centered intervention
• Inherent uncertainties
• Requires shared decision making, informed pt consent & close monitoring of effects
• Same principles that apply when drug therapy is initiated
• Not about denying effective treatments to eligible pts

Scott IA. JAMA IM May 2015 vol 175(5)
De-prescribing protocol

• Ascertain all drugs pt is taking & reasons for each one
• Consider the benefits of treatment & risk of adverse effects
• Determine which drugs can be safely discontinued
• Prioritize drugs for discontinuation
• Implement & monitor drug discontinuation

Adapted from Scott IA. JAMA IM May 2015 vol 175(5)
A medication review and deprescribing method for hospitalised older patients receiving multiple medications

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1Advanced Trainee General Medicine, Ipswich Hospital, Ipswich, 2Clinical Pharmacology, Princess Alexandra Hospital, Harlow, UK, 3Internal Medicine and Clinical Epidemiology, Princess Alexandra Hospital and 4School of Medicine, University of Queensland, Brisbane, Australia

Methods: Prospective pilot study of a convenience sample of patients aged ≥65 years admitted acutely to general medicine units in a tertiary hospital and receiving eight or more regular medications on presentation. The intervention comprised an education programme and a paper-based or computerised proforma listing clinical and medication data linked with a five-step decision support tool for selecting drugs eligible for discontinuation, which were then ceased or were being weaned by the time of discharge.
**Results:** Among 50 patients of median age 82.5 years and six co-morbidities, 186 of 542 (34.3%) regular medications were discontinued, representing a significant decrease in the median (interquartile range) number of medications per patient at discharge compared with presentation (7 (5–9) vs 10 (9–12), *P* < 0.001). Medication lists were reduced by at least two medications in 84% of patients, and by four or more in 50%. Statins, gastric acid suppressive agents, angiotensin-converting enzyme inhibitors/angiotensin receptor antagonists and inhaled bronchodilators were the most frequently ceased medications. Of 39 patients in whom follow-up status at a median of 78 days was ascertained, only 5 of 413 (1.2%) ceased medications were recommenced among three patients because of symptom relapse.

**Conclusion:** A standardised method of medication review and deprescribing may significantly reduce medication burden in a cohort of older hospitalised patients.
<table>
<thead>
<tr>
<th>Medication class</th>
<th>Patients in whom medication ceased/patients receiving medication on admission (%)</th>
<th>Patients receiving medication on admission/all patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statin</td>
<td>21/37 (57%)</td>
<td>37/50 (74%)</td>
</tr>
<tr>
<td>Gastric acid suppression</td>
<td>19/40 (48%)</td>
<td>40/50 (80%)</td>
</tr>
<tr>
<td>ACE inhibitor/ARA</td>
<td>15/31 (48%)</td>
<td>31/50 (62%)</td>
</tr>
<tr>
<td>Inhaled bronchodilators</td>
<td>14/20 (70%)</td>
<td>20/50 (40%)</td>
</tr>
<tr>
<td>Diuretic</td>
<td>12/23 (52%)</td>
<td>23/50 (46%)</td>
</tr>
<tr>
<td>Other antihypertensives</td>
<td>10/17 (59%)</td>
<td>17/50 (34%)</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>10/35 (29%)</td>
<td>35/50 (70%)</td>
</tr>
<tr>
<td>SSRI/SNRI</td>
<td>10/22 (45%)</td>
<td>22/50 (44%)</td>
</tr>
<tr>
<td>Opioid analgesic</td>
<td>9/22 (41%)</td>
<td>22/50 (44%)</td>
</tr>
<tr>
<td>Oral hypoglycaemic</td>
<td>9/15 (60%)</td>
<td>15/50 (30%)</td>
</tr>
<tr>
<td>Nitrate</td>
<td>8/11 (73%)</td>
<td>11/50 (22%)</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>8/15 (53%)</td>
<td>15/50 (30%)</td>
</tr>
</tbody>
</table>
## Table 4  Reasons for discontinuation

<table>
<thead>
<tr>
<th>Medication class (number discontinued)</th>
<th>No valid indication or part of prescribing cascade, $n$ (%)</th>
<th>Time to benefit exceeds life expectancy, $n$ (%)</th>
<th>Risk of harm exceeds benefit, $n$ (%)</th>
<th>No effect on symptoms resolved, $n$ (%)</th>
<th>Unacceptable treatment burden, $n$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins ($n = 21$)</td>
<td>1 (5%)</td>
<td>17 (81%)</td>
<td>3 (14%)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Gastric acid suppressive agents ($n = 19$)</td>
<td>14 (74%)</td>
<td>—</td>
<td>—</td>
<td>5 (26%)</td>
<td>—</td>
</tr>
<tr>
<td>ACE inhibitors/ARAs ($n = 15$)</td>
<td>2 (13%)</td>
<td>4 (27%)</td>
<td>8 (53%)</td>
<td>1 (7%)</td>
<td>—</td>
</tr>
<tr>
<td>Inhaled bronchodilators ($n = 14$)</td>
<td>10 (72%)</td>
<td>—</td>
<td>1 (7%)</td>
<td>3 (21%)</td>
<td>—</td>
</tr>
<tr>
<td>Diuretic ($n = 12$)</td>
<td>7 (58%)</td>
<td>—</td>
<td>4 (33%)</td>
<td>1 (9%)</td>
<td>—</td>
</tr>
<tr>
<td>Other antihypertensive agents ($n = 10$)</td>
<td>1 (10%)</td>
<td>2 (20%)</td>
<td>4 (40%)</td>
<td>1 (10%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Anti-platelet agents ($n = 10$)</td>
<td>6 (60%)</td>
<td>2 (20%)</td>
<td>2 (20%)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>SSRI/SNRI ($n = 10$)</td>
<td>1 (10%)</td>
<td>—</td>
<td>—</td>
<td>8 (80%)</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Opioid analgesics ($n = 9$)</td>
<td>2 (22%)</td>
<td>—</td>
<td>4 (44%)</td>
<td>3 (34%)</td>
<td>—</td>
</tr>
<tr>
<td>Oral hypoglycaemic agents ($n = 9$)</td>
<td>—</td>
<td>3 (34%)</td>
<td>3 (34%)</td>
<td>2 (22%)</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>Nitrates ($n = 8$)</td>
<td>3 (38%)</td>
<td>—</td>
<td>2 (24%)</td>
<td>3 (38%)</td>
<td>—</td>
</tr>
<tr>
<td>Benzodiazepines ($n = 8$)</td>
<td>—</td>
<td>—</td>
<td>5 (63%)</td>
<td>3 (37%)</td>
<td>—</td>
</tr>
<tr>
<td>Other psychotropic drugs ($n = 8$)</td>
<td>2 (25%)</td>
<td>—</td>
<td>2 (25%)</td>
<td>3 (38%)</td>
<td>1 (12%)</td>
</tr>
<tr>
<td>Other drugs‡ ($n = 33$)</td>
<td>11 (33%)</td>
<td>3 (9%)</td>
<td>11 (33%)</td>
<td>8 (25%)</td>
<td>—</td>
</tr>
<tr>
<td>Total number of discontinued medications ($n = 186$)</td>
<td>60 (32%)</td>
<td>31 (17%)</td>
<td>49 (26%)</td>
<td>41 (22%)</td>
<td>5 (3%)</td>
</tr>
</tbody>
</table>
De-prescribing: Hospitalists’ Role

- Communicate w/ stakeholders
  Pt, prescribing provider, nurse
- Document rationale and plan in medical record
- Monitor pt
De-prescribing: 5 medication classes

- Proton pump inhibitors
- Benzodiazepines
- Statins
- Atypical anti-psychotics
- Tricyclic anti-depressants

Proton Pump Inhibitor (PPI) Deprescribing Algorithm

**Indication still unknown?**
- mild to moderate esophagitis or GERD treated x 4-8 weeks (esophagitis healed, symptoms controlled)
- peptic ulcer disease treated x 2-12 weeks (from NSAID; H. pylori)
- upper GI symptoms without endoscopy; asymptomatic for 3 consecutive days
- ICU stress ulcer prophylaxis treated beyond ICU admission
- uncomplicated H. pylori treated x 2 weeks and asymptomatic
- Barrett’s esophagus
- chronic NSAID users with bleeding risk
- severe esophagitis
- documented history of bleeding GI ulcer

**Why is patient taking a PPI?**
- If unsure, find out if history of endoscopy, if ever hospitalized for bleeding ulcer or if taking because of chronic NSAID use in past, if ever had heartburn or dyspepsia

**Recommend Deprescribing**
- strong recommendation (from systematic review and GRADE approach)
- evidence suggests no increased risk in return of symptoms compared to continuing higher dose, or (daily until symptoms stop) (1/10 patients may have return of symptoms)
- decrease to lower dose
- stop PPI
- continue PPI or consult gastroenterologist if considering deprescribing

**Monitor at 4 and 12 weeks**
- If verbal:
  - heartburn
  - dyspepsia
  - regurgitation
  - epigastic pain
- If non-verbal:
  - loss of appetite
  - weight loss
  - agitation

**Use non-drug approaches**
- Avoid meals 2-3 hours before bedtime; elevate head of bed; address if need for weight loss and avoid dietary triggers

**Manage occasional symptoms**
- over-the-counter antacid, H2RA, PPI, alginate pm (e.g., Tums®, Rolaid®, Zantac®, Olex®, Gaviscon®)
- H2RA daily (weak recommendation – GRADE; 1/5 patients may have symptoms return)

**If symptoms relapse:**
- If symptoms persist x 3 – 7 days and interfere with normal activity:
  1) Test and treat for H. pylori
  2) Consider return to previous dose
# Proton Pump Inhibitor (PPI) Deprescribing Notes

## PPI Availability

<table>
<thead>
<tr>
<th>PPI</th>
<th>Standard dose (healing) (once daily)*</th>
<th>Low dose (maintenance) (once daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole (Losec®) - Capsule</td>
<td>20 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Esomeprazole (Nexium®) - Tablet</td>
<td>20 mg or 40 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Lansoprazole (Prevacid®) - Capsule</td>
<td>30 mg</td>
<td>15 mg</td>
</tr>
<tr>
<td>Dexlansoprazole (Dexilant®) - Tablet</td>
<td>30 mg or 60 mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>Pantoprazole (Tecta®, Pantoloc®) - Tablet</td>
<td>40 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>Rabeprozole (Pariet®) - Tablet</td>
<td>20 mg</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

## Engaging patients and caregivers

Patients and/or caregivers may be more likely to engage if they understand the rationale for deprescribing (risks of continued PPI use; long-term therapy may not be necessary), and the deprescribing process.

## PPI side effects

- When an ongoing indication is unclear, the risk of side effects may outweigh the risk of benefit.
- PPIs are associated with higher risk of fractures, *C. difficile* infections and diarrhea, community-acquired pneumonia, vitamin B12 deficiency and hypomagnesemia.
- Common side effects include headache, nausea, diarrhea and rash.

## Tapering doses

- No evidence that one tapering approach is better than another.
- Lowering the PPI dose (for example, from twice daily to once daily, or halving the dose, or taking every second day) OR stopping the PPI and using it on-demand are equally recommended strong options.
- Choose what is most convenient and acceptable to the patient.

## On-demand definition

Daily intake of a PPI for a period sufficient to achieve resolution of the individual’s reflux-related symptoms; following symptom resolution, the medication is discontinued until the individual’s symptoms recur, at which point, medication is again taken daily until the symptoms resolve.

## Legend

- **a** Non-erosive reflux disease
- **b** Reflux esophagitis
- **c** Symptomatic non-erosive gastroesophageal reflux disease
- **d** Healing of erosive esophagitis
- + Can be sprinkled on food

* Standard dose PPI taken BID only indicated in treatment of peptic ulcer caused by *H. pylori*; PPI should generally be stopped once eradication therapy is complete unless risk factors warrant continuing PPI (see guideline for details).

## Key

- **GERD** – gastroesophageal reflux disease
- **NSAID** – nonsteroidal anti-inflammatory drugs
- **H2RA** – H2 receptor antagonist
- **SR** – systematic review
- **GRADE** – Grading of Recommendations Assessment, Development and Evaluation
De-prescribing Barriers

- Difficulty making decisions to stop drugs
- Worry about stopping drugs started by other prescribers
- Limited knowledge about how to stop drug
- Concern about drug withdrawal effects

We spend a lot of time thinking about how to start medications and surprisingly little time thinking about when to stop them. Let's do something about this. Lives depend on it.

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