The Art & Science of Deprescribing
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Disclosures and Conflicts of Interest
I am currently funded by the Cancer Prevention and Research Institute of Texas (functional status in cancer survivors) and the Health Care Service Corporation (deprescribing in UTP clinics).

I will not discuss off-label use of medications or products.

Learning Objectives
1. Paraphrase seminal deprescribing literature
2. Describe common clinical scenarios where deprescribing is appropriate
3. Identify policies and procedures that encourage deprescribing during care transitions
4. Apply knowledge and skills to clinical cases dealing with deprescribing of benzodiazepines and opioids

Older patients are the highest consumers of medication

- Polypharmacy – significant and consistent risk factor for adverse drug reactions (ADRS), falls, dizziness, hospitalizations
- High use of inappropriate medications
- ADRs in 10-35% ambulatory older patients, responsible for 9% hospital admissions

We all agree that there will be a lot of older people in the future.


Deprescribing

Definition:
- The systematic process of identifying and reducing or 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, current level of functioning, life expectancy, values, and preferences.

Geriatrics fellowship on a single slide

Significant heterogeneity in survival

Guiding Principles for the Care of Older Adults with Multimorbidity

- Patient Preferences
- Interpreting the Evidence
- Prognosis
- Treatment Complexity and Feasibility
- Optimizing Therapies and Care Plans

Evidence for the harms of polypharmacy

- All observational studies, mostly cohort and longitudinal cohort, some case-control
  - Mixed results, some with poor adjustment for comorbidity
- Increasing med number associated with
  - Falls and dizziness
  - Adverse drug events
  - Hospitalizations
- Message: polypharmacy is harmful

Strategies to reduce polypharmacy

- Prescribe fewer medications and/or stop more medications.
- Avoid high risk / low benefit meds >> “inappropriate” drugs.
- Avoid drugs that frequently lead to adverse reactions >> “high risk drugs”.
- Approach all prescribing with deprescribing in mind.

Deprescribing – When medications have...

- Clear harms
- Potential adverse drug effect
- High risk or inappropriate medications
- Uncertain benefits
- Multimorbidity and polypharmacy
- Life-limiting or debilitating illness
- Change in goals of care
- When the medication is part of a prescribing cascade

Scott. JAMA Intern Med. 2015;175(5):827-34.
Boyd, CM, Fortin M. Public Health Reviews, 2011.

The Process of Deprescribing

1. Ascertain that all drugs the patient is currently taking and the reasons for each one.
2. Consider overall risk of drug-induced harm in individual patients in determining the required intensity of deprescribing intervention.
3. Assess each drug for its eligibility to be discontinued.
4. Prioritize drugs for discontinuation.
5. Implement and monitor drug discontinuation regimen.

Scott et al. JAMA Internal Medicine 2015.

Prescribing cascades

NSAID >> anti-HTN
Acetylcholinesterase inhibitor >> pacemaker
Acetylcholinesterase inhibitor >> bladder anticholinergic

The Process of Deprescribing

- It’s as easy as: “123-ABC”
  1. Purpose of each medication
  2. How is the patient using medication
  3. “How’s that working for you?”

A. Adverse effects
B. Benefits/burdens of drug therapy
C. Conversations

Tools that aid in deprescribing

- Criteria/lists of inappropriate medications
- Deprescribing algorithms and pamphlets

How to be a “deprescriber”

- Pick a drug
- Pick a tool
- Pick a patient population
- Pick a clinical scenario
- Pick a transition

Benefits of Deprescribing

• Reduces unnecessary burden
• Reduces unnecessary cost
• Improves quality care
• Is part of patient-centered care

Patient attitudes to deprescribing

Case 1: “Are you trying to kill her?!”

78 year old woman residing in the nursing home
• Medical history: Alzheimer’s disease, coronary artery disease, atrial fibrillation, history of breast cancer
• Repeated falls in the past 3 months

Current medications
• Donepezil 10mg once daily
• Memantine 10 mg twice daily
• Lisinopril 40 mg daily
• Atorvastatin 20 mg QHS
• Warfarin 5 mg every evening
• Multivitamin daily
• Iron sulfate 325 mg daily
• Calcium and Vit D tablets TID

Case 1: “Are you trying to kill her?!”

• Which medications would you deprescribe?
• How would you approach the conversation?

Donepezil 10mg once daily
Memantine 10 mg twice daily
Lisinopril 40 mg daily
Atorvastatin 20 mg QHS
Warfarin 5 mg every evening
Multivitamin daily
Iron sulfate 325 mg daily
Calcium and Vit D tablets TID

Total medication burden increases as time to death shortens.

Anti-Dementia Drugs: Evidence for Deprescribing

• Cholinesterase inhibitors are efficacious for mild to moderate Alzheimer’s dementia, while memantine has a small benefit at six months in moderate to severe Alzheimer’s dementia
• Most trials had a treatment duration of 6 months to 1 year, however most were only 12-24 weeks
• Cochrane doesn’t say much for those near or at the end of life:
  • Can be expensive agents for hospice
Comparing scales for dementia

- Note correlation between decline of functional scores and cognitive scales

Effect of ChEI discontinuation of neuropsychiatric symptoms over trial duration

<table>
<thead>
<tr>
<th>Study</th>
<th>SMD (95% CI)</th>
<th>N Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holman, et al 2004</td>
<td>-0.46 (-0.87 to -0.05)</td>
<td>22.7</td>
</tr>
<tr>
<td>Howard, et al 2012</td>
<td>-0.20 (-0.53 to 0.13)</td>
<td>34.01</td>
</tr>
<tr>
<td>Johannsen, et al 2006</td>
<td>-0.34 (-0.65 to -0.04)</td>
<td>61.28</td>
</tr>
<tr>
<td>Overall (I^2 = 0.79, p=0.02)</td>
<td>-0.32 (-0.64 to -0.01)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Anti-Dementia Drugs: The Opposing View

- Previous literature has suggested negative impact upon discontinuation of ChEI on patients and their care
- "Cholinesterase inhibitor discontinuation in patients with Alzheimer's disease: a meta-analysis of randomized controlled trials."
  - Meta-analysis including investigating the effects of ChEI discontinuation on patients with AD
  - Results: 18 studies reviewed – 5 ChEI discontinuation randomized controlled studies (N=521 continued and N=532 discontinued; following patients for 1.5-24 months)

Guidelines to deprescribe in dementia?

- No evidence-based guidelines.
- AChE or memantine >12 months, consider a deprescribing trial if:
  1. Cognition or function is worse
  2. No benefit during treatment
  3. Severe/end-stage dementia
- Deprescribe if the indication is not for dementia
- Patient preference
- How?

Communication Techniques

Prescribers

- Utilize Situation/ Background/ Assessment/ Recommendations format:
  - Highlight goals of care, functional status and/or prognosis, and where risks outweigh benefits

Patients and Families and/or Caregivers

- Communication techniques:
  - Shared-decision making
  - "Now that I know [you] I recommend...."

Pharmacist calls prescriber...

- "As you know..." (Lynn McPherson technique)
- "Did you know that your patient is taking...?" (Cara Tannenbaum technique)
Case 1 discussion

Case 2: “My husband is in a fog.”

83 year old man recently discharged after hospitalization for pneumonia

- Medical history: hypertension, spinal stenosis, depression, anxiety, insomnia, chronic kidney disease, chronic lung disease
- Has been independent until the last 6 to 9 months and increasingly forgetful, needing help with bills, taking medications incorrectly

Current Medications

- Amitriptyline 75 mg at bedtime
- Amlodipine 5 mg daily
- Lisinopril 5 mg daily
- Aspirin daily
- Hydrocodone with acetaminophen twice daily
- Alprazolam 0.5 mg daily (has escalated to 3 times daily)
- Zolpidem 10 mg at bedtime
- Quetiapine 25 mg TID added in the hospital for agitation

Case 2: What would you do?

- How many drugs would you stop?
- How many simultaneously?
- How would you prioritize?

Amitriptyline 75 mg at bedtime
- Amlodipine 5 mg daily
- Lisinopril 5 mg daily
- Aspirin daily
- Hydrocodone with acetaminophen twice daily
- Alprazolam 0.5 mg daily (has escalated to 3 times daily)
- Zolpidem 10 mg at bedtime
- Quetiapine 25 mg TID added in the hospital for agitation

Case 2: Medication chronology

Antipsychotic deprescribing

- For use in acute delirium, consult psychiatrist...

Available at https://www.deprescribingnetwork.ca/

Anticholinergic and sedative burden

- Drug Burden Index: an estimate of a drug’s anticholinergic and sedative burden (scaled 0-1)
- Increasing DBI associated with poorer functional and cognitive scores
- Cumulative exposure over 20 years also associated with poorer cognitive and physical function

Hilmer et al., Arch Intern Med 2007
Wouters et al., J Gerontol A, Jan 2019.
Sedative deprescribing: the EMPOWER study

- 261 participants taking benzodiazepines recruited from 30 community pharmacies in Canada
- 86% completed 6 month follow-up
- 27% stopped the benzodiazepine in the intervention group compared to 5% of the control group


Case 2 discussion

Case 3: “Do I have enough meds?”

79 year old man with multimorbidity
- Referred to geriatrics for fatigue
- Medical history: coronary artery disease, hypertension, chronic kidney disease, hyperlipidemia, Type 2 diabetes mellitus
- Tells you that he is lethargic and never has any energy. Occasionally has nausea.

Current Medications
- Atorvastatin 80mg at bedtime
- Metformin 1000mg BID,
- Sliding scale insulin
- Lisinopril 20 mg daily
- Ferrous sulfate 325 mg BID
- Cholecalciferol
- Calcium acetate
- Aspirin
- Folic acid
- Vitamin B complex

Case 3: “Do I have enough meds?”

- Are there any medications eligible for deprescribing?
- Wait – I thought we were being patient-centered. Does he have enough meds?

- Atorvastatin 80mg at bedtime
- Metformin 1000mg BID,
- Sliding scale insulin
- Lisinopril 20 mg daily
- Ferrous sulfate 325 mg BID
- Cholecalciferol
- Calcium acetate
- Aspirin
- Folic acid
- Vitamin B complex

Deprescribe?

We are supposed to add ezetimibe according to the guidelines...

For primary prevention – we are on our own.
Guidelines will not help us.

Grundy et al Circulation 2018
Quality of life in the statin discontinuation trial

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Mean AUC</th>
<th>AUC Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Discontinued Statin</td>
<td>Continued Statin</td>
<td></td>
</tr>
<tr>
<td>Quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>6.12</td>
<td>6.53</td>
<td>6.95</td>
<td>0.18 (0.28 to 0.64)</td>
</tr>
<tr>
<td>Physical</td>
<td>5.19</td>
<td>5.43</td>
<td>5.51</td>
<td>-0.08 (-0.43 to 0.26)</td>
</tr>
<tr>
<td>Psychomotor</td>
<td>7.21</td>
<td>7.08</td>
<td>6.99</td>
<td>0.99 (0.02 to 0.88)</td>
</tr>
<tr>
<td>Wellbeing</td>
<td>7.02</td>
<td>7.17</td>
<td>7.09</td>
<td>-0.32 (0.80 to 0.64)</td>
</tr>
<tr>
<td>Support</td>
<td>8.31</td>
<td>8.38</td>
<td>7.86</td>
<td>-0.53 (0.26 to 0.09)</td>
</tr>
<tr>
<td>Total</td>
<td>6.98</td>
<td>7.11</td>
<td>6.89</td>
<td>-0.26 (0.02 to 0.53)</td>
</tr>
</tbody>
</table>

Statin withdrawal associated with bad outcomes

<table>
<thead>
<tr>
<th>Primary outcome event</th>
<th>Statin withdrawal group, n (%)</th>
<th>Non-statin withdrawal, n (%)</th>
<th>OR (95% CI)</th>
<th>Adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>17 (60.0)</td>
<td>18 (39.0)</td>
<td>7.39 (1.02, 56.6)</td>
<td>4.64 (1.46, 14.91)</td>
</tr>
<tr>
<td>Disability</td>
<td>30 (65.2)</td>
<td>9 (20.9)</td>
<td>7.08 (2.73, 18.37)</td>
<td>8.67 (5.05, 24.65)</td>
</tr>
</tbody>
</table>

* Adjusted for age and the Global Gait Score at admission.

Figure 1: HgbA1c (%) values for the eight patients...

<table>
<thead>
<tr>
<th>Duration (Months)</th>
<th>HgbA1C (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>12</td>
<td>4</td>
</tr>
</tbody>
</table>

p=0.4 (95% CI, 1.1-0.5)

Anti-Diabetic Medications: The Opposing View

- Must consider treatment target: primary versus secondary prevention versus symptom control
  - Previous studies have suggested an increase in mortality with discontinuation, or “looser” guidelines
- “Discontinuation of antihyperglycemic therapy and clinical outcomes after acute myocardial infarction in older patients with diabetes”
  - Retrospective study of 24,953 Medicare beneficiaries with diabetes discharged after hospitalization for AMI
  - Primary outcome: time to death within 1 year of discharge; secondary outcomes: time to first rehospitalization within 1 year for AMI, heart failure, and all causes
  - Assessed via multivariable Cox proportional hazard models

<table>
<thead>
<tr>
<th>Unadjusted Analysis</th>
<th>Multivariable Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hazard Risk</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.47 (1.32-1.64)</td>
</tr>
<tr>
<td>MI readmission</td>
<td>0.83 (0.69-0.93)</td>
</tr>
<tr>
<td>Heart failure readmission</td>
<td>0.96 (0.87-1.06)</td>
</tr>
<tr>
<td>All-cause readmission</td>
<td>0.93 (0.86-1.00)</td>
</tr>
</tbody>
</table>

Mortality rates and readmissions after stopping diabetes medications in patients with myocardial infarction

Case 3 Discussion

Statins:
- Must consider treatment target: if primary prevention, ok to deprescribe. Do not deprescribe "shortly" after event
- Consider time-until-benefit and estimated remaining life expectancy (does this patient meet the surprise question?)

Antidiabetic Medications:
- Must consider treatment target: is our goal really HgbA1C? Do not deprescribe “shortly” after event
- Consider time-until-benefit: previous better control helps overall
Case 4: “He’s a drug abuser”

- 68 year old man admitted from the nursing home for altered mental status
- Diagnosed with delirium on admission
- Medical history includes Alzheimer’s disease, hypertension, chronic low back pain, hypothyroidism, weight loss

Current Medications
- MS Contin 100mg PO q12h
- Oxycodone IR 30mg PO q4h PRN (unsure how many he takes)
- Haloperidol 0.5mg TID
- Lorazepam 0.5mg PO TID PRN (unsure how many)
- Pantoprazole 40mg PO once daily
- Acetaminophen 500mg TID
- Vitamin D 1000 IU daily
- Gabapentin 100mg HS
- Senna 1 tab QHS
- Docusate 100 mg bid
- Levophedrine 100 mg daily
- Metoprolol 40mg TID
- Prochlorperazine 10 mg TID PRN (unsure of how many...)

Case 4: “He’s a drug abuser”

- How many drugs would you deprescribe?
- Where should we start?
- MS Contin 100mg PO q12h
- Oxycodone IR 30mg PO q4h PRN (unsure how many 5ig takes)
- Haloperidol 0.5mg TID
- Lorazepam 0.5mg PO TID PRN (unsure how many)
- Pantoprazole 40mg PO once daily
- Acetaminophen 500mg TID
- Vitamin D 1000 IU daily
- Gabapentin 100mg HS
- Senna 1 tab QHS
- Docusate 100 mg bid
- Levophedrine 100 mg daily
- Metoprolol 40mg TID
- Prochlorperazine 10 mg TID PRN (unsure of how many...)

The “HAM” Sandwich

- Considered necessary medications for palliative care patients, commonly prescribed
  - Helps treat many symptoms, and low cost
- However, considered “high risk” medications
  - Major classes associated with drug-induced adverse reactions, 30 day readmissions, etc.

Opioids and Benzos – Evidence for Deprescribing

- Nebulous goal of treatment, limited efficacy
- Little evidence to support the use of opioids in chronic low back pain
- Increased risk of opioid-induced respiratory depression in elderly patients:
  - 2.8 times higher in patients aged 61-70 years old, up to 8.7 times higher in patients over age 80
- Increased risk with co-administration with BZDs
- Risk of opioid abuse, or other opioid-specific consequences (being triggered with prescription medications)
- 40% of palliative care patients have risk factors for opioid misuse

Efficacy of treating pain to reduce behavioral disturbances in residents of NH with dementia

- Cluster, RCT of stepwise analgesic treatment
  - 1. APAP -> 2. oral morphine (up to 20mg/day) -> 3. TD buprenorphine -> 4. PG
- N=352 NH resident with moderate to severe dementia, and clinically significant behavioral disturbances
- Primary outcome: Agitation (scores via CMAI)
- Results: agitation was significantly reduced in the intervention group at 8 weeks (p<0.001)

Opioids and BZDs: The Opposing View

- Pain is real for this patient
  - There are age-associated changes in the elderly with pain. Overall, pain threshold increases, but tolerance to pain decreases
  - Prevalence of pain in patients with AD: ~25%, however this may be underestimated
  - Per JAGS, opioids can be appropriate for elderly patients
  - By removing these agents, you could increase the risk of delirium
Case 4: *Overall Clinical Pearls*

**Opioids and benzodiazepines:**
- Consider your treatment target or goal
- What other non-controlled substances, or non-pharmacological interventions, could be helpful?
- Consider time receiving medications, in terms of withdrawal risk
- Shared-decision making is necessary
- Monitoring plan is necessary

**Is there a good opioid deprescribing tool?**
- Deprescribe if:
  - No improvement in pain or function
  - Doses >50 MME/day
  - Signs of substance use disorder
  - Has overdose or adverse events
  - Early warning signs for overdose risk
- How?
  - 10% per week
  - Stop when taking < once per day

Available at cdc.gov

**Possible strategies for Case 4**

Let's just focus on this hospitalization
- Is delirium caused by any meds?
- How to handle the opioids?
- What about other sedating and anticholinergic meds?

- Voltaren 100 mg PO q12h
- Oxycodone IR 30 mg PO q4h PRN (unsure how many he takes)
- Haloperidol 0.5 mg tid
- Lorazepam 0.5 mg PO tid PRN (unsure how many)
- Pantoprazole 40 mg PO once daily
- Acetaminophen 500 mg tid
- Vitamin D 1000 IU daily
- Gabapentin 100 mg hs
- Senna 1 tab QHS
- Docusate 100 mg bid
- Levothyroxine 100 mcg daily
- Metoprolol 200 mg qd
- Prochlorperazine 10 mg tid PRN

Let's make a plan for the next 6 months
- Opioids
- Sedatives
- Anticholinergics
- Others?

- MS Contin 100 mg PO tid
- Oxycodone IR 30 mg PO q4h PRN (unsure how many)
- Haloperidol 0.5 mg tid
- Lorazepam 0.5 mg PO tid PRN (unsure how many)
- Pantoprazole 40 mg PO once daily
- Acetaminophen 500 mg tid
- Vitamin D 1000 IU daily
- Gabapentin 100 mg hs
- Senna 1 tab QHS
- Docusate 100 mg bid
- Levothyroxine 100 mcg daily
- Metoprolol 200 mg qd
- Prochlorperazine 10 mg tid PRN (unsure how many)
The Barriers of Deprescribing

- Unclear Patient Population
- Psychological Connections with Medications
- Risk of Adverse Withdrawal Events
- Time, and Confusion Over Discipline/Specialty
- Lack of Evidence


Deprescribing – communication is key

- Taking advantage of opportune moments
- Contextualizing patient attitudes, goals, preferences
- The importance of “priming the pump”
- Negotiating prescriber priorities
- Understanding that stopping omeprazole is different from stopping oxycodone


The Power of the Pharmacist

- 489 patients 65 and older recruited in community pharmacies
- Pharmacist gave brochure to patient and note to physician
- Goal to reduce 4 Beers drugs (glyburide, sedative-hypnotics, first-gen antihistamines, or NSAIDs)
- 6 month follow up: 43% of intervention group stopped the meds compared to 12% control group

JAMA. 2018;320:1889-1898.

Another strategy for another talk...


Key Points

- Deprescribing is a systematic process to reduce or discontinue medications as part of patient-centered care >> pharmacists are the ideal team members to lead deprescribing efforts.
- It is uncertain which populations, medications, and settings are ideally suited for deprescribing >> start where you are.
- Deprescribing efforts need to be tailor to the patient and to the medication and situation >> one size does not fit all.

Thank you