Deprescribing: An Antidote to Polypharmacy in Older Adults

Lori Martin-Plank, PhD, FNP-BC, NP-C, GNP-BC, FAANP, FNAP
Objectives

- To present information on safe deprescribing of medications in older adults with polypharmacy and also to discuss situations where “rational polypharmacy” is acceptable and contributes to the overall efficacy of the pharmacotherapeutic plan of care.

- Following this presentation, participants will be able to define polypharmacy and list one way that it contributes to adverse drug reactions in older adults.

- Participants will be able to explain the basic concepts of safe deprescribing and apply these to examples supplied by the presenter.
Keys to Understanding Older Adults

- Heterogeneity—older adults are the most heterogeneous population group
- Know general principles of aging physiology versus pathophysiology
- Significance of lab values and changes with aging
- Need to individualize treatment
- For any new symptom, consider ADR (adverse drug reaction) in differential
Key Issues with Physiological Changes

- Interrelationship of all systems increases vulnerability to illness and to drug interactions
- Reduced physiological reserve of most body systems, particularly cardiac, respiratory, and renal.
- Reduced homeostatic mechanisms → failure to adjust regulatory systems such as temperature control and fluid and electrolyte balance.
- Impaired immunological function → increased infection, increase in autoimmune diseases
Drug Use in Older Adults

- Comprise 8.5% of the world population; will increase to 17% by 2050.
- Consume 34% of all Rx drugs
  - 91% regularly use at least one Rx med (F>M)
  - 29% regularly use 5 or more Rx meds
  - 50% nursing home patients use 9 or more meds
- Big consumers of OTC, dietary supplements, and Rx drugs
  - Consume 40% of all OTC medications
  - 52% currently use dietary supplements and Rx drugs (F>M)
  - 46% currently use OTC and Rx medications (M>F)
- Vulnerable to ADE (adverse drug events) and drug interactions
Most common health conditions and most commonly used prescription drugs (US)

1. hydrocodone/acetaminophen
2. Simvastatin
3. Lisinopril
4. Levothyroxine
5. Azithromycin
6. Metformin
7. Amlodipine
8. Amoxicillin
9. Hydrochlorothiazide

Majority (70%) have 1-4 comorbidities

Source: FDA 3/17
What are Pharmacokinetics and Pharmacodynamics?

”Quick and Dirty”

- Pharmacokinetics—what the body does with the drug
  - Absorption
  - Distribution
  - Metabolism
  - Elimination

- Pharmacodynamics—what the drug does to the body
Altered Pharmacokinetics

Age-related changes in physiology and organ function result in altered pharmacokinetics: Absorption, Distribution, Metabolism (Biotransformation), Elimination

- Absorption: Primarily unchanged
- Little clinical significance for commonly used drugs
- Iron, calcium, zinc chelate with quinolones, levothyroxine and L-dopa, decreasing absorption

Gastric motility is decreased; gastric pH is increased BUT...

Add a PPI—what happens? Antisecretory drug -> reduced absorption of azole antifungals, cephalosporin; increased absorption of digoxin and nifedipine, increased bioavailability of alendronate.
Altered Pharmacokinetics

- Decreased protein binding, increased bioavailability (e.g., warfarin, phenytoin, aspirin, digoxin)

- Body fat increases, lean muscle mass and body water decrease (serum creatinine is unreliable)
Altered Pharmacokinetics

- Metabolism (Biotransformation):
- Metabolic clearance by the liver may be reduced (CYP-450 enzyme activity is unpredictable)
- Drugs with a high rate of extraction by the liver may have increased bioavailability (e.g., warfarin, tricyclic antidepressants, propranolol)

Liver shrinks in size, hepatic blood flow decreases by ~40%, decrease in Phase 1 CYP-450 action
Altered Pharmacokinetics

- **Elimination:**
  - Decreased renal function (40-50%) may lead to higher serum drug levels and longer drug half-life
  - Reduced renal clearance of active metabolites may enhance therapeutic effect or risk of toxicity (e.g., digoxin, lithium, aminoglycosides, vancomycin)

Decrease in renal mass, formation of cysts, decreased blood flow, GFR and tubular function.

- **Serum creatinine not a reliable predictor of renal function in older adults due to decreased muscle mass**
- **MDRD superior to Cockcroft-Gault in older adults**
Pharmacodynamic Alterations

- Age-related changes resulting in sensitivity to certain classes of drugs place the elderly at risk for adverse drug reactions
- CNS depressants (e.g., benzodiazepines) resulting in delirium, confusion, agitation and sedation
- Anticoagulants and hemorrhage (e.g., in combination with NSAIDs, salicylates)
- Alpha-blockers and various antihypertensive medications resulting in orthostatic hypotension
- Anticholinergic medications resulting in dry mouth, constipation, urinary retention, blurred vision, confusion
What is Polypharmacy?

- Poly=many; Pharmacy refers to drugs
- No real consensus definition? >5 drugs
- Can include potentially inappropriate medications (PIMS)
  - Underprescribing
  - Overprescribing
  - Misprescribing

- Strong association between polypharmacy and adverse drug reactions, increased morbidity and mortality in older adults
Is Polypharmacy Always A Problem?

Rational Polypharmacy (risk outweighs benefit): difficult to treat epilepsy, mental health multimorbidity
What are some Factors Contributing to Polypharmacy in Older Adults?

- Multiple chronic health conditions
- Addition of an acute health problem on pre-existing chronic condition
- Confusion in following clinical guidelines
- Patient is seeing several specialty providers, lack of coordination of care
- Undisclosed use of OTC preparations, herbals, dietary supplements
What are some Factors Contributing to Polypharmacy in Older Adults?

- Patient does not understand what medications are for, may be taking them incorrectly
- Failure to reconcile medications after a hospitalization (sent home or back to nursing home without explicit instructions or “resume previous medication”)—handoffs/ transitions
- Patient is unable to afford medications, so does not fill prescriptions
- Sharing of medications—”this really helped me, why don’t you try it”
- Direct to consumer advertising (in countries where permitted)
Other Considerations Related to Polypharmacy

- Prescribing Cascade—ADR from one drug goes unrecognized and an additional drug is prescribed, e.g. donepezil can cause urinary incontinence—so an antimuscarinic such as oxybutinin is prescribed for the incontinence.
- Side effect of antimuscarinics, antihypertensives (vasodilator, ACEs, beta-blockers), opioid analgesics is dizziness, so meclizine is prescribed.
- Drug-drug interaction: ACE and ARB prescribed together
- Dose related problem
- Failure to realize need for renal dosing
Other Considerations Related to Polypharmacy

- **PIMS:** Potentially Inappropriate Medicines
- Anticholinergics
- Atypical Antipsychotics
- Benzodiazepines
- Digoxin
- Warfarin (not inappropriate but multiple drug-drug interactions)
Characteristics of the Optimal Medication Prescription

- Maximum Efficacy
- Safety
- Evidence-based
- Cost-effective
- Minimal side-effects
- Easy to self-administer
- Respects patient preferences
Resources for Evaluating Drug Regime

- **BEERS list** (new list has accompanying article with suggested substitutions—2018 currently online for public comment)
- **STOPP/START**
- **FORTA**
- See Kauffman reference on systematic review of current tools to assess inappropriate prescribing
- **Collaboration with clinical pharmacist**
- **Clinical Guidelines**
- **American Geriatrics Society Guiding Principles for the Care of Older Adults with Multimorbidity**
Approach to the evaluation and management of the older adult with multimorbidity.

- Inquire about the patient’s primary concern (and that of family and friends, if applicable) and any additional objectives for visit.
- Conduct a complete review of care plan for person with multimorbidity. OR Focus on specific aspect of care for person with multimorbidity.
- What are the current medical conditions and interventions? Is there adherence to and comfort with treatment plan?
  - Consider patient preferences.
- Is relevant evidence available regarding important outcomes?
  - Consider prognosis.
- Consider interactions within and among treatments and conditions.
- Weigh benefits and harms of components of the treatment plan.
  - Communicate and decide for or against implementation or continuation of intervention/treatment.
- Reassess at selected intervals for benefit, feasibility, adherence, alignment with preferences.

https://www.americangeriatrics.org/
Deprescribing—an Antidote to Polypharmacy

- **Deprescribing**—the systematic and deliberate discontinuation, tapering, or dose reduction of drugs in conjunction with the patient/family and utilizing evidence-based resources.

- Originated in Europe, recent press in the US

- Canadian Group with tool: MedStopper
  - [http://medstopper.com](http://medstopper.com)

- Several small studies trialing different methods—single drug or multiple drugs

- Pharmacist and provider community primarily involved; goal is to engage primary care providers to participate.

- Subscribes to need for continuous and ongoing re-evaluation of older adult, changes in condition and goals for care, risk-benefit of drug—e.g. high dose statin in 90 year old patient with advanced dementia, ongoing PPI
Deprescribing—an Antidote to Polypharmacy

- Safeguards include consent/buy in from patient/family; need to carefully focus on scientific basis, e.g. Less is More, new events masquerading as another illness but really an adverse drug reaction
- Families/patient may be resistant, feel that they are being abandoned
- Instructions in s/s of any adverse events due to discontinuation—e.g. shortness of breath, chest pain
- Regular monitoring of patient during chronic management visits (3 months initially)
- Restart medication if adverse event detected
- In some cases, dose reduction rather than discontinuation is the goal
- Some meds MUST be tapered—benzodiazepines, psychotropics, certain opiates, etc
Considerations in Deprescribing

- **Statins**—what is the life expectancy of the patient? What is the indication?
- **Bisphosphonates**—how long has the patient been treated (5yrs max, reconsider?), any fractures?
- **Antihypertensives**—monitor BP—is the drug still necessary?
- **Laxatives**—consider natural remedy such as prune juice, bran
- **PPIs**—short term use only
- **Cholinesterase inhibitors**—are they effective (advanced dementia); if not d/c due to antimuscarinic SE
- **NSAIDS**—serious thought
- **Antipsychotics**—consider behavioral interventions
Advanced Practice Nursing
Interventions to Decrease Polypharmacy

- Parsimonious prescribing—for every drug, consider the risks and benefits, necessity. Keep it simple; less is more.
- Consider the patient who will be taking the drug
- Look at the broader picture—what alternatives are available in lieu of pharmacotherapy
- If you are not the prescriber, don’t hesitate to question or initiate a change (clinical inertia, tend to add on but not discontinue existing)
- Communicate: patient/family, other providers
- Educate or delegate (home health nurse)
Advanced Practice Nursing Interventions to Decrease Polypharmacy

- Review meds at every visit; periodic “brown bag” session
- Discuss with patient/family: risk/benefit
- Age of patient/life expectancy/goals of treatment
- Alternatives to pharmaceuticals—lifestyle, holistic
- Discontinue unnecessary drugs
- Consider dose reduction
Cases from Practice
### Drug/Disease Grid

<table>
<thead>
<tr>
<th>Drug/Dosage (frequency, route)</th>
<th>Disease/Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albuterol sulfate 2.5 mg/3 mL solution inhale 3 mL by nebulization route QID</td>
<td>COPD</td>
</tr>
<tr>
<td>Alendronate 70 mg PO Q week</td>
<td>Osteopenia</td>
</tr>
<tr>
<td>Allopurinol 300 mg PO daily</td>
<td>GOUT</td>
</tr>
<tr>
<td>Amlodipine 3 mg PO daily</td>
<td>HTN, CAD</td>
</tr>
<tr>
<td>Aspirin 325 mg PO daily</td>
<td>Cardiovascular protection, CAD</td>
</tr>
<tr>
<td>Colchicine 0.6 mg 2 tab PO initially, then 1 tab in 1 hour PRN</td>
<td>PRN GOUT</td>
</tr>
<tr>
<td>Fluoxetine 20 mg take 3 capsules PO daily in am</td>
<td>Major Depressive Disorder</td>
</tr>
<tr>
<td>Gabapentin 300 mg take 3 capsules PO BID</td>
<td>Chronic neuropathic pain</td>
</tr>
<tr>
<td>Ipratropium bromide 0.02% solution inhale 2.5 mL by nebulization route q6h</td>
<td>COPD</td>
</tr>
<tr>
<td>Lisinopril 40 mg PO daily</td>
<td>HTN</td>
</tr>
<tr>
<td>Levocetin 40 mg take 2 tab PO daily with evening meal</td>
<td>HLD, DM-II, CAD</td>
</tr>
<tr>
<td>Magnesium oxide 250 mg tab take 2 tab PO q10</td>
<td>Hypomagnesemia</td>
</tr>
<tr>
<td>Meclizine 25 mg PO TID PRN</td>
<td>PRN Dizziness</td>
</tr>
<tr>
<td>Metformin 500 mg tab take 2 tab PO BID</td>
<td>DM-II</td>
</tr>
<tr>
<td>Methadone 5 mg tab take 1 tab PO q OTHER day and 1 tab BID q OTHER day alternating for pain</td>
<td>Chronic pain syndrome</td>
</tr>
<tr>
<td>Montelukast 10 mg PO daily in the evening</td>
<td>Seasonal allergies, COPD</td>
</tr>
<tr>
<td>Nitroglycerin 0.4 mg sublingual take 1 at first sign of attack, may repeat q5min until relief; if pain persists after 3 tab in 15 min, prompt medical attention recommended</td>
<td>PRN angina</td>
</tr>
<tr>
<td>Omeprazole 20 mg capsule take 2 capsules PO daily before a meal</td>
<td>GERD</td>
</tr>
<tr>
<td>Ranitidine 150 mg PO BID PRN</td>
<td>PRN heartburn</td>
</tr>
<tr>
<td>Saline Nasal Mist 0.65% spray aerosol instill 1-2 spray by nasal route q2-4q PRN</td>
<td>PRN nasal congestion</td>
</tr>
<tr>
<td>Sinemet 25mg-100mg tab take 1 tab PO BID</td>
<td>Restless leg syndrome</td>
</tr>
<tr>
<td>Victoza 1.8 mg subcutaneous daily</td>
<td>DM-II, obesity</td>
</tr>
</tbody>
</table>

### Problem List

- COPD exacerbation
- Allergic rhinitis
- Uncontrolled HTN
- DM-II
- CAD
- HLD
- Morbid obesity
- Tobacco use

### 65 yr old female
<table>
<thead>
<tr>
<th>DRUG</th>
<th>Disease/Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin 2.5mg daily PO</td>
<td>Anticoagulation for Atrial Fibrillation &amp; Heart Failure</td>
</tr>
<tr>
<td>Metoprolol Tartrate 12.5mg twice daily PO</td>
<td>Hypertension &amp; Heart Failure</td>
</tr>
<tr>
<td>Digoxin 125mcg daily PO</td>
<td>Heart Failure &amp; Atrial Fibrillation</td>
</tr>
<tr>
<td>Furosemide 20mg twice daily PO</td>
<td>Hypertension &amp; Heart Failure</td>
</tr>
<tr>
<td>Potassium Chloride ER 10mg daily PO</td>
<td>Prevention of Potassium Depletion</td>
</tr>
<tr>
<td>Simvastatin 10mg daily PO</td>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Symbicort inhaler 80-4.5mcg/ACT 2 puffs twice daily</td>
<td>Maintenance corticosteroid/LABA for COPD</td>
</tr>
<tr>
<td>ProAir Respiclick inhaler 90mcg/ACT every 4 hours as needed</td>
<td>Rescue albuterol for bronchospasm related to COPD</td>
</tr>
<tr>
<td>Oxygen 2-3 lpm continuous, 4 lpm at night and with exertion</td>
<td>COPD</td>
</tr>
<tr>
<td>Triazolam 0.125mg at bedtime as needed</td>
<td>Insomnia</td>
</tr>
<tr>
<td>Acetaminophen 500mg every 6 hours as needed PO</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Nitroglycerin 0.4mg as needed SL</td>
<td>Heart Disease</td>
</tr>
<tr>
<td>Estrace 0.01% vaginal cream</td>
<td>Recurrent UTI</td>
</tr>
<tr>
<td>Cranberry supplement</td>
<td>Recurrent UTI</td>
</tr>
<tr>
<td>Probiotic</td>
<td>Recurrent UTI and Antibiotic Associated Diarrhea</td>
</tr>
<tr>
<td>DRUG (dosage, frequency, route)</td>
<td>Disease/Indication</td>
</tr>
<tr>
<td>---------------------------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Ocuvite adult 50+ oral, 1 tablet PO QD</td>
<td>Supplement, No indication</td>
</tr>
<tr>
<td>Aspirin 81mg EC tablet, 1 tablet PO QD</td>
<td>Heart disease</td>
</tr>
<tr>
<td>Coenzyme Q10, 100mg, capsule, 1 tablet PO QD</td>
<td>Supplement, No indication</td>
</tr>
<tr>
<td>Premarin 0.3mg tablet, 1 tablet PO twice a week</td>
<td>Postmenopausal</td>
</tr>
<tr>
<td>Nexium 40mg, 1 tablet PO QD</td>
<td>Gastroesophageal reflux disease</td>
</tr>
<tr>
<td>Fish oil 1,000mg capsule, 1 tablet PO QD</td>
<td>Hypercholesteremia, heart disease</td>
</tr>
<tr>
<td>Lasix 20mg, 0.5 tablet PO QD PRN for edema</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Lisinopril 40 mg, 1 tablet PO QD</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Loratadine 10mg, 1 tablet PO QD</td>
<td>Allergic Rhinitis</td>
</tr>
<tr>
<td>Metformin XR 500mg, 2 tablets PO BID with meals.</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>Naproxen Sodium 220mg capsule, 1 tablet PO BID with meals.</td>
<td>Arthritis</td>
</tr>
<tr>
<td>Metoprolol 50mg, 24 hour tablet, 1 tablet PO QD</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Pravastatin 40mg, 1 tablet PO QD</td>
<td>Hypercholesteremia</td>
</tr>
<tr>
<td>Januvia 100mg, 1 tablet PO QD</td>
<td>Diabetes Mellitus</td>
</tr>
</tbody>
</table>

67 yr old F, HTN, heart disease (1 stent), DM type 2, GERD, allergic rhinitis, osteoarthritis, “postmenopausal” and post hysterectomy, bilateral knee replacements
Selected References


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