PolyPharmacy

Learning Objectives

- The audience will be able to:
  - Identify pharmacokinetic & pharmacodynamic aspects of pharmacotherapy
  - Discuss these aspects as they relate to changes with age
  - Identify patients/medications, polypharmacy, errors, and adverse drug event correlations
  - Implement strategies to “get it right” in an effort to mitigate potential correlations

Polypharmacy

- Definitions:
  - A range of 2 to 11 or more medications (Masnoon et al.)
  - Use of a large number of medications, commonly considered to be the use of five or more (Express Scripts)
  - Five or more medications used daily (CMS)
  - Taking 5 or more pills a day or currently taking medications for 5 or more conditions (CDC)

CDC Statistics

- >30% of US seniors are taking 5 or more medications
- 22.4% of US adults aged 40-79 use 5 or more medications in the past 30 days

CDC Statistics

- Over the last 10 years:
  - The percentage of Americans who took at least one prescription drug in the past month increased from 44% to 48%
  - The use of two or more drugs increased from 25% to 31%
  - The use of five or more drugs increased from 6% to 11%
- In 2007-2008, 1 out of every 5 children and 9 out of 10 older Americans reported using at least one prescription drug in the past month
- Those who were without a regular place for health care, health insurance, or prescription drug benefit had less prescription drug use compared with those who had these benefits
- The most commonly used types of drugs involved in these statistics included:
  - Asthma medications (in children)
  - Central nervous system stimulants (in adolescents)
  - Antidepressants (in middle-aged adults)
  - Cholesterol lowering drugs (in seniors)

Additional Statistics

- Those 65 year and older represent 12.6% of the US population, approximately one in eight Americans
- The elderly account for nearly 30% of the nation’s health care expenditures and 25% of drug expenditures
- A survey of non-institutionalized participants found that 12% of women aged above 65 years took at least 10 medications and 23% took at least five prescription drugs
- The average US nursing home resident uses seven different medications each month, and about one-third of residents have monthly drug regimens of nine or more medications
- By 2030, it is estimated that one in five Americans (71.5 million) will be over the age of 65 years

New Mexico Statistics

• By 2030, it is estimated that New Mexico will have 33% (300,000) seniors taking 5 or more medications (4th on the state rankings)
• In case you are wondering why pharmacists are so busy, here’s a possible answer: They are filling a lot of prescriptions each month, for nearly half the population of the US with key performance indicators measuring output.

Pharmacokinetics Review

- Absorption
- Distribution
- Metabolism – varies based on age, sex, individual variation/genetic polymorphism, enterohepatic circulation, intestinal flora, nutrition, age
- Excretion

• * Changes with age:
  - Increase in body fat relative to skeletal muscle (diazepam)
  - Decreased drug metabolism due to natural renal and hepatic decline (fentanyl)
  - Increased drug concentrations due to prolonged half lives (lithium)

Pharmacodynamics Review

- Receptor affinity
- Receptor number
- Response
- Homeostasis

• * Changes with age:
  - Increase in response to benzodiazepines and opioids (alprazolam, oxycodone)
  - Decrease in adrenergic 2 receptors results in decreased responsiveness (clonidine)
  - Impairment of homeostasis such as BP regulation, bladder functionality, electrolyte balance (confusion)
Disease States that Affect Pharmacokinetics and/or Pharmacodynamics

- Renal Failure, Liver Disease, Congestive Heart Failure
  - Increases distribution
  - Decreases elimination

Factors Contributing to Polypharmacy

- Increasing age
- Multiple symptoms and/or medical problems
- Over prescribing
- Multiple providers or lack of PCP coordination
- Multiple pharmacies
- Drug regimen changes/Guideline changes
- Hoarding of medications by patient
- Self-treatment by patient

Indicators of Polypharmacy

- Prescribing medications with no indication
- Use of medications in same drug category
- Concurrent use of interacting medications
- Prescribing drugs contraindicated in elderly
- Ordering inappropriate dosages or not maximizing current therapies
- Using a drug to treat an adverse drug event
### Additional & Potential Indicators of Polypharmacy
- Transitions of care mismanaged
- Discharge review incomplete
- Medication reconciliation incomplete
- Lack of electronic health information interface
- COVID barriers to care
  - Worried about appt. cancellations
  - Inability to tele-visit
  - Online medication sales

### Case (NetCE.com)
- 82 years of age with a history of CHF, glaucoma, hypertension, and osteoarthritis.
- Her current medications are furosemide, potassium, lisinopril, metoprolol, aspirin, timolol maleate opth. solution, acetaminophen (prn), multivitamin, and a calcium/vitamin D supplement.
- She has an appointment with a new orthopedic physician.
- During the appointment, the patient complains of persistent arthritic pain in her knee and is prescribed, meloxicam (7.5 mg per day) for pain and inflammation.

### Choices
- Meloxicam
- Ibuprofen
- Any NSAID
- Topicals
- Tylenol (max.)
- Tramadol

### Discussion
- Meloxicam is a good choice, as it should help to ameliorate symptoms, however, from a cardiac standpoint, this is a risky approach due to the potential side effect of fluid retention and its effect on the heart.
- In general, NSAIDs can be dangerous for an individual of and 82 year old patient.
- NSAIDs (including meloxicam, but also over-the-counter options like ibuprofen) have been issued warnings by the U.S. Food and Drug Administration for the increased risk of:
  - Serious and potentially fatal cardiovascular and thrombotic events, including myocardial infarction and stroke
  - Serious adverse gastrointestinal events such as bleeding, ulcer, and intestinal perforation (higher in seniors)

### Answer/Outcome
- Pharmacist faxes PCP prior to dispensing, makes the patient come back at a later time.
- PCP advises against NSAID and instead, creates a pain management plan that minimizes the potential risks.
- Plan:
  - Patient was taking acetaminophen as needed, averaging up to one dose daily, this is increased to twice daily extended-release acetaminophen (650 mg)
  - For breakthrough pain, tramadol 25 mg every four hours (as needed) is prescribed
  - Another option considered was the topical anti-inflammatory diclofenac gel, which would have fewer side effects than systemic agents
  - Patient is scheduled with a physical therapist to create a safe exercise plan, including strengthening and range-of-motion exercises

### Case Quiz
- Meloxicam
- Ibuprofen
- Any NSAID
- Topicals
- Tylenol (max.)
- Tramadol
The Prescribing Cascade

INITIAL CONDITION | THERAPY | NEW SYMPTOM | SUBSEQUENT RX
--- | --- | --- | ---
ARTHRITIS | NSAID | ↑ Blood Pressure | BP Med
DEPRESSION | Tricyclic Antidepressant | Constipation | Antipsychotic
AGITATION | Antihypertensive | Cerebral Func. Syndrome | Parkinson’s Med

Gurwitz JH. P&T. 1997

Potentially Inappropriate Medications (PIM)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Rationale</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergics (1st Generation)</td>
<td>Risk of confusion, dry mouth and constipation</td>
<td>Avoid</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td></td>
<td></td>
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<tr>
<td>Promethazine</td>
<td></td>
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<tr>
<td>Antiparkinson</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benztrapine</td>
<td>Not recommended for prevention of extrapyramidal symptoms with antipsychotics</td>
<td>Avoid</td>
</tr>
<tr>
<td>Trihexyphenidyl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Highly anticholinergic</td>
<td>Avoid</td>
</tr>
<tr>
<td>Hallucinarian</td>
<td></td>
<td></td>
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<tr>
<td>Anti-infective</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>Potential for pulmonary toxicity, nephrotoxicity and peripheral neuropathy</td>
<td>Avoid when CrCl &lt; 30mL/min or long term use</td>
</tr>
</tbody>
</table>


BEERS and PIMS

- Prescribing that poses more risk than benefit to the individual
- Using medications that either have no clear evidence-based indication, carry a substantially higher risk of ADE, or not cost-effective


Potentially Inappropriate Prescribing

- The cost of medication related problems has been estimated to be:
  - $76.6 billion to ambulatory care
  - $20 billion to hospitals
  - $4 billion to nursing home facilities
- If medication-related problems were ranked as a disease by cause of death, it would be the fifth leading cause of death in the US,

Case

- 78 year old man, resides in a nursing facility.
- One year ago, he fell and fractured his left hip and underwent surgical repair. He returned to the nursing facility, completed rehabilitation, and regained most of his prior function.
- After the surgery, was prescribed warfarin to prevent deep vein thrombosis (DVT) after surgery.
- During a routine visit, it was discovered that patient is still being administered warfarin, the warfarin was never discontinued after the appropriate duration after the hip fracture repair.

Discussion

- This is an example of using the right drug but not using it for the correct duration.
- After surgery, warfarin is usually indicated for approximately two to three months or until activity/ambulation has increased to a point that the risk of DVT is reduced.
- There is a substantial burden of treatment with warfarin, including weekly evaluations of prothrombin time/international normalized ratio (PT/INR), adverse reactions, interactions, and increased risk of bleeding and brain hemorrhage, especially for patients with a history of falls.

Outcome

- PCP called and warfarin was discontinued.
- When medications are DC’d, plans to monitor should be put in place.
- There is shared responsibility for this error between the prescriber/healthcare provider and the facility, and the consultant pharmacist.

Mitigation

- Tools developed by expert panels:
  - Drug Burden Index
  - FORTA (Fit for the Aged) List
  - STOPP/START Criteria
  - Medication Appropriateness Index
  - Others
    - Adherence strategies/pharmacy automation
    - Individual drug class/De-Prescribing Criteria

De-Prescribing Quiz

1. Is there an indication for the drug?
2. Is the medication effective for the condition?
3. Is the dosage correct?
4. Are the directions correct?
5. Are the directions practical?
6. Are there clinically significant drug–drug interactions?
7. Are there clinically significant drug–disease/condition interactions?
8. Is there unnecessary duplication with other drugs?
9. Is the duration of therapy acceptable?
10. Is the drug the least expensive alternative compared to others of equal utility?

Screening Tool of Older Persons’ Potentially Inappropriate Prescriptions (STOPP)

- STOPP is comprised of 65 clinically significant criteria for potentially inappropriate prescribing in seniors:
  - includes drug-drug and drug-disease interactions
  - arranged according to relevant physiological systems
  - each criterion is accompanied by a concise explanation as to why potentially inappropriate prescribing is recommended.


Screening Tool to Alert to the Right Treatment (START)

- START consists of 22 evidence-based prescribing indicators to identify prescribing omissions (medication indicated, but not prescribed).
  - Cardiovascular system
    - Warfarin in the presence of chronic atrial fibrillation, where there is no contraindication to warfarin
  - Respiratory system
    - Inhaled steroid in moderate-to-severe asthma or COPD, where reversibility of airflow obstruction has been shown
  - Gastrointestinal system
    - Proton pump inhibitor in the presence of chronic severe gastro-esophageal acid reflux
  - Endocrine system
    - ACE inhibitor or Angiotensin Receptor Blocker in diabetes with nephropathy


Select Safer Alternatives

<table>
<thead>
<tr>
<th>STOPP</th>
<th>START</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisone</td>
<td>Allopurinol</td>
</tr>
<tr>
<td>Unnecessary corticosteroids</td>
<td>DMARD (Rheumatoid Arthritis)</td>
</tr>
<tr>
<td>Acetaminophen, topical (Osteoarthritis)</td>
<td>Inhaled corticosteroids and/or bronchodilator (COPD)</td>
</tr>
<tr>
<td>Opioids</td>
<td>Acetaminophen or NSAIDs (Mild/Moderate pain)</td>
</tr>
<tr>
<td>Non-selective Beta Blockers (COPD)</td>
<td>Atenolol (Cardioselective Beta Blockers)</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Anxiety – low dose shorter acting (Lorazepam), SSRIs or SNRIs</td>
</tr>
<tr>
<td>Sleep – Low dose Temazepam or Zolpidem</td>
<td>Glyburide</td>
</tr>
</tbody>
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Strategies to Optimize Prescribing

- Computerized interventions (soft edits, reports)
- Colleague interventions (collaborations, continuing education)
- Educational interventions (learn sessions, journal clubs, patient calls)

- Caution, Pushback Examples:
  - Fax Backs
  - Videos

Strategies to Increase Adherence

- Short-term Treatment
  - Counseling on importance
  - Written instructions
  - Tools for reminder

- Long-term Treatment
  - Counseling on importance/long term benefits
  - Written instructions
  - Simplify regimen
  - Tools for reminder
  - Cueing to daily events
  - Reinforce/Reward
  - Patient self monitoring
  - Involve family/significant others

Haynes et al. JAMA, 288:2880-81

Additional Adherence Strategies

- Counseling on importance/long term benefits
- Written instructions
- Tools for reminder
- Involve family/significant others

Haynes et al. JAMA, 288:2880-81

Additional Pharmacy Efforts

- 1) ProAir to Ventolin or Proventil or Albuterol
- 2) Qvar to Flovent
- 3) All nonsedating 2nd gen antihistamines to cetirizine
- 4) All statins to simvastatin as first line

Medication Characteristics; Making them at High Risk for Potential ADE

- Negative:
  - Extensive oxidative metabolism (P450)
  - Many active metabolites
  - Highly protein bound
  - Lipophilic

For example: Cimetidine, CYP450 enzyme inducer; can increase both plasma concentration and elimination half-life.

For example: Phenytoin, CYP450 inhibitor, slows or stops the chemical action of a CYP450 by binding with the enzyme before it can do its job.

CDC Data

ISMP Top Ten
Case

• A patient is currently taking iron therapy for anemia and azithromycin for a URI and complains about heartburn, you want to treat.

Outcome

• Minerals like calcium, magnesium, and iron therapy, interfering with the absorption of certain antibiotics.
• Space the calcium carbonate 2 hours before and 4 hours after food.
• Histamine blockers, like famotidine, decrease stomach acid, and therefore interfere with iron therapy.

Case

• Your patient notes that they cannot take their levothyroxine before breakfast on an empty stomach due to GI sensitivity.

Outcome

• Absorption of levothyroxine is greatly affected by food and even when drinking coffee within an hour.
• Wait 60 minutes after taking levothyroxine to drink your coffee.
• Food and enteral tube feedings interfere with the absorption of levothyroxine as well.

Cannabis Instead of Polypharmacy?

https://www.projectcbdo.org/

Summary

• Identification of potential polypharmacy is key to its decrease in the US.
• Many tools are available for use in the mitigation of polypharmacy.
• A stepwise approach to avoidance of polypharmacy, medication errors, and adverse drug events may be beneficial to your practice.