Polypharmacy and the Elderly
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Objectives
- Recognize factors leading to polypharmacy in the elderly
- Define inappropriate medications for elderly patients
- Describe tools to screen patients for polypharmacy
- Describe best practices for limiting Adverse Drug Events (ADEs) in “necessary medications”

Polypharmacy, what is it?
“The administration of many drugs together”
- Wide range of definitions
- No consensus definition
- 4, 5, 9 or more chronic medications
- Prescription medications
- Over-the-counter (OTC) medications
- Vitamin supplements
- Herbal products

Polypharmacy definition
- Most common in literature:
  - Medication does not match diagnosis
  - Many medications and duplication of medications
  - Inappropriate dosing frequency (excessive duration, dose too low, dose too high), medication prescribed to treat a side effect
  - The term “inappropriate” often occurs in definitions
  - Number of medications taken routinely
  - “Hyperpharmacotherapy”
  - Excessive use of drugs for treatment of disease
  - Carries a negative connotation
  - Medication Underutilization
  - Omission of an indicated and potentially beneficial medication for the treatment or prevention of disease

Institute of Medicine Report
Retooling for an Aging America: Building the Healthcare Workforce
- Requires significant overhaul to care for estimated 70 million adults > 65 by 2030
- No profession currently trains # of geriatric specialists needed
- Currently <1% of medical professionals are certified or have specialty training in geriatrics.
- Schools and organizations need to collaborate to ensure core competencies to care for older adults with geriatric syndrome

Geriatric Syndromes
- Polypharmacy
- Dementia
- Imbalance/Immobility/Falls
- Functional Decline
- Urinary Incontinence
- Malnutrition
- Frailty
Pharmacokinetic Changes in The Elderly
- Hepatic blood flow drops by 40%
- Half of elderly have some form of CKD
- Heart failure patients can further exacerbate these decreases
- First-pass clearance decreases in elderly
  - Warfarin
  - Benzodiazepines
  - Opiates

Pharmacokinetics
- Absorption: least affected by age
- Distribution: highly lipid-soluble medications stay in the body longer
- Metabolism: 30-40% reduction as a person ages
- Elimination:
  - Age 20: creatinine clearance of 100 to 120ml/min
  - Age 40: creatinine clearance starts to decrease by 10% every 10 years of age
  - Age 75: renal clearance can be reduced by up to 50%
  - When creatinine clearance falls below 30ml/min, the excretion of medications through the kidney is greatly reduced

Pharmacokinetics
- Protein binding changes
  - Malnutrition
  - Dentures
  - Food preparation differences
  - Dietary restrictions
  - Substance abuse affecting metabolism
  - Up to 10% of elderly use significant alcohol

Growth of the Elderly Population
- Represent nearly 42 million
  - 13.3% of total population
- Population has increased 18% since 2000
- At 65th birthday have median life expectancy of 18-20 years
- Over one-third of elderly received 90% of income from social security

Elderly Population and Medications
- Receive more than 50% of all prescription medications
- More than 90% of non-institutionalized patients are on at least 1 Rx med
- Most who engage in healthcare system take 6-8 medications
- Comorbidities such as HTN, DM, Heart failure that require multiple medications
- OTCs
  - Elderly purchase 40% of OTCs
  - Use of OTCs is 3-fold higher in elderly
Medication Use in Older Adults
- 50% of community-dwelling elderly
  - Take 5 or more Rxs and OTCs
- 20% of community-dwelling elderly
  - Take 10 or more Rxs and OTCs
- 30% of hospitalizations in elderly
  - Medication-related admission

Prescribing in the Elderly has unique challenges
- Pre-marketing drug trials exclude elderly participants
- Approved doses may not be appropriate for the elderly.
- Special Pharmacokinetics:
  - Absorption, Distribution, Metabolism, Excretion
- Special Pharmacodynamics:
  - Physiologic Effects of the Drug
  - Frailty
  - What percent of participants have normal albumin?

Consequences of polypharmacy
- Cost
  - CMS estimates $50 billion annually
  - Co-Pays, Coverage gap (refills fall off at the end of the year)
- Adverse Drug Events
  - Risk increases with multiple comorbidities, use of high risk drugs (i.e. warfarin), and increasing number of meds
- Poor Adherence
  - ADRs
  - Complex regimens
  - Poor Outcomes
  - Hip fractures, hospitalizations, death

Adverse Drug Events
- World Health Organization: “Unintended and undesired effects of a medication at a normal dose”
- Five primary categories
  - Adverse Drug Reaction
  - Medication Error
  - Therapeutic Failure
  - Adverse Drug Withdrawal Event
  - Overdose

Adverse Drug Reactions
**RISK OF ADVERSE DRUG REACTIONS:**

<table>
<thead>
<tr>
<th>Medications</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>13%</td>
</tr>
<tr>
<td>5</td>
<td>58%</td>
</tr>
<tr>
<td>7 or more</td>
<td>82%</td>
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Additional medications lead to greater incidence of drug interactions.

Adverse Drug Reaction
- Of those taking > 5 drugs for one year, 35% have an adverse drug event
- Elderly 2-3 times more likely to have ADR from any one drug
- 28% have at least one ADR while hospitalized
  - Doubles the length of stay
- 65% of LTCF residents experience at least one ADR in a 4 year period
- 80% of adverse drug events are treated with another drug
  - Prescribing Cascade!
Common Prescribing Cascade
- Ibuprofen → hypertension → anti-hypertensive therapy
- Metoclopramide → parkinsonism → Sinemet
- Amlodipine → edema → furosemide
- Gabapentin → edema → furosemide
- Ciprofloxacin → delirium → risperidone
- Lithium → tremor → propranolol
- Bupropion → insomnia → mirtazapine
- Donepezil → urinary incontinence → oxybutynin
- Amiodarone → tremor → lithium
- Venlafaxine → tremor → diazepam
- Narcotic → constipation → senokot
- Senokot → diarrhea → imodium
- Furosemide → hypokalemia → Slow K
- Cimetidine → low B12 → B12 supplement

Etiology of Polypharmacy
- Medications added to treat acute illness during hospitalization
- Continued upon discharge
- Not needed, or not needed in as high a dose
- Hospital Formulary switches over home meds
- Care Delivery by Multiple Physicians
- Transitional Care, poor reconciliation

Etiology of Polypharmacy
- Medication Prescribing Cascade
  - New drug prescribed to treat old drug’s side effects
  - Sharing of Medications and Diversion
  - No “short fills” for Narcotics
  - Use of Over the Counter Medications
  - Adherence to multiple Clinical Practice Guidelines

Etiology of Polypharmacy
- Fear of discontinuing medications
  - Belief that discontinuing a medications will lead to catastrophic events
  - Stopping isosorbide will cause an acute MI
  - Stopping furosemide will lead to flash pulmonary edema.
  - Participant who has donepezil restarted will not return to the functional level achieved before discontinuation.
  - It was prescribed by a “specialist” who is more familiar with treatment of given disease entity

3 Kinds of Polypharmacy
- Pseudo-polypharmacy
- Appropriate polypharmacy
- Inappropriate polypharmacy

How To Deal with Polypharmacy
Pseudo-Polypharmacy

- Record shows patient to be taking more medication than patient really takes
- Often old medications in possession
- Medication reconciliation
  - Find out what patient really takes
  - Discard old medications

Appropriate Polypharmacy

- Multiple medications, all of which are appropriate for recognized indications
- Many conditions are now best treated with multiple medications
- Examples
  - Heart Failure
  - Hypertension
  - Diabetes
- Under treatment is also a problem

Commonly Underused Medications in Elderly

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Most common underused meds (% underuse)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute MI</td>
<td>Nitrates (66%), aspirin (30%), beta-blockers (14%)</td>
</tr>
<tr>
<td>COPD</td>
<td>Inhaled anticholinergic bronchodilators (66%)</td>
</tr>
<tr>
<td>Depression</td>
<td>SSRI (72%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Ace inhibitors (53%), oral hypoglycemics (16%)</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>Ace inhibitors (32%)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Calcium (70%)</td>
</tr>
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Appropriate Polypharmacy

- Do not withhold polypharmacy if they are ...
  - Indicated and effective for the patients condition
  - Not interacting unfavorably with the patient’s other medications

Inappropriate Polypharmacy

- Patient takes more medication than needed/safe
  - Inappropriate for older adults
  - Interact with other medications
  - Ineffective for diagnosis
  - Duplicate therapy

Methods for Decreasing Polypharmacy

- Professional
- Educational activities for providers or patients
- Organizational
- Polypharmacy clinic
- Financial
- Incentive programs
- Regulatory interventions
Tools to Help Decrease Polypharmacy

- Beers Criteria
- STOPP Criteria
  - Screening Tool of Older Persons' potentially inappropriate Prescriptions
- START Criteria
  - Screening Tool to Alert Doctors to Right Treatment

Beers Criteria

- Originally published in 1991 for residents of nursing homes
- Consensus list of 53 medications or medication classes potentially inappropriate for adults.
  - Risk > Benefits
  - Think twice before prescribing/recommending
  - Then think again...
- Tool for geriatric teams

Beers Criteria 2012

- 53 Medications assigned to one of three criteria
- Drugs that are “Potentially Inappropriate”
  - Barbiturates, Chlorpropamide
- Drugs “Potentially Inappropriate because of Drug/Disease or Drug/Syndrome interaction
  - NSAIDs and CHF
- Those that should be used with caution
  - Dabigatran (Pradaxa) in patients >75 yrs. Risk of bleeding greater than with warfarin
- Some of the Medications listed are OTCs

Beers Criteria

- Most commonly used tool
- Available at http://www.americangeriatrics.org
- App available at iTunes for free, but there are some in-app purchases

Key Medications on Beers Criteria

- Anticholinergics and Cholinesterase Inhibition
- Antihistamines
  - Sedation
  - Cognitive impairment
  - Dry mouth
  - Constipation
  - Urinary Retention
  - Examples
  - Diphenhydramine (Benadryl)
  - Hydroxyzine (Atarax)
Key Medications on Beers Criteria

- Long-Acting Benzodiazepines
  - Cognitive dysfunction
  - Falls
  - Addiction/Withdrawal
  - Examples
    - Diazepam (Valium)
    - Flurazepam (Dalmane)
    - Chlordiazepoxide (Librium)

- Tricyclic Antidepressants
  - Anticholinergic
  - Cardiac toxicity
  - Orthostatic hypotension
  - Examples
    - Amitriptyline (Elavil)
    - Doxepin (Sinequan)

- Antipsychotic medications
  - First Generation
    - Movement disorders
  - Second Generation
    - Hyperlipidemia, weight gain, diabetes
  - Both Generations - FDA warning
    - Death from heart disease, infections
  - Examples
    - Haloperidol (Haldol)
    - Olanzapine (Zyprexa)

- NSAIDS- Ibuprofen, Naproxen
  - 3,000 people > 65 years die each year in the US from complications of NSAIDS
  - GI bleeding/perforations
  - Renal impairment
  - Fluid restriction (BP, HF)
  - Digoxin
  - If essential, use low dose (0.125mg/day)

Beers Criteria

- Medical Conditions
- Anorexia: CNS stimulant drugs, amphetamines
- Chronic constipation: CCBs, anticholinergics
- Depression: long-acting benzodiazepines
- Gastric Ulcers: NSAIDs
- Cognitive impairment: anticholinergics, antispasmodics
- Parkinson’s Disease: metoclopramide, antipsychotics

STOPP

- Screening Tool of Older Persons’ Potentially inappropriate Prescriptions
- Comprised of 65 clinical criteria
- Potentially inappropriate medications are listed by organ system
  - Focused on meds commonly used in geriatric population in Europe
- Some overlap with Beers criteria
STOPP: Screening Tool for Older People's potentially Inappropriate Prescriptions. The following drug prescriptions are potentially inappropriate in patients aged ≥65 years of age:

Cardiovascular System
1. Digoxin at a long-term dose ~125μg/day with impaired renal function (increased risk of toxicity).
2. Loop diuretics for decompensate heart failure only if no clinical signs of heart failure (no evidence of efficacy, compression history usually more appropriate).
3. Loop diuretics as first-line monotherapy for hypertension (see more effective alternatives available).
4. Thiazide diuretics with a history of gout (may exacerbate gout).
5. Beta-blocker with Chronic Obstructive Pulmonary Disease (COPD) risk of increased bronchospasm.
7. Use of diuretic or warfarin with NYHA Class III or IV heart failure (may worsen heart failure).
8. Calcium channel blockers with chronic obstruction (may exacerbate obstruction).

START

• Screening Tool to Alert doctors to Right Treatments
• Developed in conjunction with STOPP guidelines in European treatments for elderly patients
• Composed of 22 criteria by organ system
• Identify correct treatments for elderly patients

Question: Why the Difference?
“Co-mission versus Omission?”
(IF a Prescriber can start a medication to treat a condition not fearing a possible adverse drug reaction, (e.g. a rash), knowing that discontinuing the offending medication will solve that problem if it occurs.....

WHY THEN....do prescribers fear discontinuing medications (e.g. digoxin) when a frail elderly participant is having anorexia and weight loss over concerns of precipitating CHF or rapid Atrial Fibrillation?

Discontinuing Medications.
What is the risk?
• Broad based studies on the subject are limited
• 26% of drug discontinuation resulted in worsening of the underlying disease state
• Recurrence of angina
• Re-elevation of blood pressure
• 4% were associated with withdrawal reaction
• Beta-Blockers
• Benzodiazepines

Discontinuing Medications:
• Tapering of medication preferable
• Exceptions include
  • Dangerous signs or symptoms attributable to drug
  • Clinical Inertia in the participant
  • Future opportunities for drug modification limited
• Rule of thumb:
  • Drugs can be tapered at the same rate at which they were titrated up upon initiation.
Discontinuing Medications

- Common Drugs Requiring Tapering
  - Opioids
  - Beta-Blockers
  - Clonidine
  - Gabapentin
  - Selective Serotonin Reuptake Inhibitors
  - Serotonin-Norepinephrine Reuptake Inhibitors
  - Tricyclic Antidepressants

Strategies for Medication Reduction

If medication prescribed for relief of symptoms, consider a “drug holiday” to assess if med is still needed.

- Is the SSRI still needed a year after being started?
- Is the PPI still needed to treat GERD or ulcer?
- Is the Anticholinergic given for urge incontinence really reducing the frequency of urination...that much? If always incontinent anyway, why use?
- Is the Cholinesterase Inhibitor still improving cognition or behavioral issues in a clinically obvious way?

Strategies for Medication Reduction

Check for evidence of adherence. If not being used, why prescribe the medication?

- Are there several Salmeterol/Fluticasone (“Advair”) inhalers unused in the house?
- Are the number of pills remaining in the vials matching the refill date?
- Does the patient admit to not taking certain meds?
- For those patients on narcotics, has a random urine drug screen been done to rule out diversion?

Strategies for Medication Reduction

- Take time at the Annual/Semi-Annual Reassessment for critical review of all medications
- Ask the patient if he/she would like their medication burden decreased.
- Ask the patients if they feel they are taking too much medication.
- You may be surprised!! Not everyone is in love with their medications
- Be positive: Let the patient know that medication reduction will likely make them feel better

Starting a New Medication

- Must this be added or could an existing medication dose be increased?
- Given the medication burden the patient already has, is it necessary?
- Is the medication being given to be in compliance with a given Clinical Practice Guideline? Are you treating the person or the disease?
- Can an existing medication’s dose be therefore decreased or eliminated?
- Can the Beta-Blocker dose be stopped when Diltiazem is added to treat Atrial Fibrillation?
Case Study Review

Case Study 1: Mrs. D

- 77 year old obese woman with diabetes, high blood pressure, heart failure, moderately severe kidney disease, high cholesterol, heartburn, severe knee arthritis, burning neuropathy in her feet, glaucoma, depression, and insomnia.
- In addition to her primary doctor, she is seen by an endocrinologist, cardiologist, neurologist, psychiatrist, and ophthalmologist.

Mrs. D’s Medications

- Metformin 1000 mg BID
- Glipizide 5 mg daily
- Metoprolol 50 mg BID
- Lisinopril 40 mg daily
- Furosemide 20 mg BID
- Simvastatin 40 mg BID
- Amitriptyline 25 mg qHS
- Duloxetine 20 mg daily
- Clonazepam 0.5 mg BID
- Gabapentin 600 mg TID
- Ranitidine 150 mg BID
- Acetaminophen with hydrocodone (Vicodin) 500mg/5mg QID PRN
- Timolol 0.5%, 1 drop to both eyes daily
- Diphenhydramine 25 mg at bedtime (Sominex)

Are There Potentially Inappropriate Medications?

- Metformin 1000 mg BID
- Glipizide 5 mg daily
- Metoprolol 50 mg BID
- Lisinopril 40 mg daily
- Furosemide 20 mg BID
- Simvastatin 40 mg BID
- Amitriptyline 25 mg qHS
- Duloxetine 20 mg daily
- Clonazepam 0.5 mg BID
- Gabapentin 600 mg TID
- Ranitidine 150 mg BID
- Acetaminophen with hydrocodone (Vicodin) 500mg/5mg QID PRN
- Timolol 0.5%, 1 drop to both eyes daily
- Diphenhydramine 25 mg at bedtime (Sominex)

Why Potentially Inappropriate?

- Confusion
- Potentially lethal if develops infection
- Timolol may add to effect of metoprolol → lower HR and BP

Why Don’t Providers Pick This Up?

- Narrow focus on specialty – unaware of best treatment of other medical conditions
- Poor communication among doctors
- Primary provider may not know about drugs prescribed by specialist
- Not aware of the age-associated side-effects and drug interactions
- Primary provider defers to specialist
Case 2: Mrs. F

- Your 68-year-old female patient presents to your office for a check-up. Her history is significant for:
  - Type 2 DM, HTN, dyslipidemia, hypothyroidism
- In reviewing the chart with the patient, she states that she does not use any herbal products. However, she confirms currently taking the following medications:

  - Aspirin, 81 mg daily
  - Atenolol, 25 mg daily
  - Atorvastatin, 20 mg daily
  - Calcium carbonate, 600 mg BID
  - Conjugated estrogen, 1.25 mg daily
  - Folic acid, 1 mg daily
  - Gemfibrozil, 600 mg BID
  - Glyburide, 5 mg BID
  - Metformin, 1,000 mg BID
  - Hydrochlorothiazide, 25 mg daily
  - Levothyroxine, 50 mcg daily
  - Lisinopril, 10 mg daily
  - Micronase, 5 mg daily
  - Multivitamin daily
  - Potassium chloride, 8 mEq daily
  - Rosiglitazone, 4 mg BID
  - Synthroid, 25 mcg daily
  - Vitamin E, 400 IU daily

  Confusion between generic and trade names of drugs resulted in this patient taking 2 different duplicate medications:
  - glyburide and Micronase, which is the trade name for glyburide
  - levothyroxine and Synthroid, which is the trade name for levothyroxine
  - Calcium carbonate and multivitamin
- Duplication occurred when the patient was recently discharged from the hospital and received new prescriptions.
- Note: admission to the hospital is a known risk factor for increasing the number of both appropriate and inappropriate medications, as well as for errors in patients’ overall medication regimens.

Final Thoughts on Polypharmacy

- Potential for severe side effects and iatrogenic illnesses
- Increased risk of ADEs, toxicity and numerous interactions
- Possible inefficacy of treatment
- Sometimes, it’s just “more harm than good”
Polypharmacy: The Good

- Combining drugs: often a way to treat multiple symptoms arising from one condition
- Terminally ill patients are dependent on polypharmacy
- The elderly and patients with multiple comorbidities may experience improved quality of life
- Overall, polypharmacy is widespread and not only limited to elderly patients
- The risks of polypharmacy can be substantially diminished by close monitoring and collective responsibility of all involved (nurses, advanced practice healthcare providers, patients/caregivers, pharmacists)

References

