Polypharmacy and the Elderly

Christopher M. Bland, Pharm.D.
Critical Care Pharmacist/Infectious Diseases Specialist
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 ADEs in “necessary” medications
Patient Case

• 74 year old female reports to her Coumadin clinic appointment. She was discharged from the hospital at 8:30 PM the previous night after being admitted for an episode of Afib with RVR. She pulls two different pill boxes out of her bag and states that she is totally confused.
Patient Case continued

• Looking exhausted she explains that she is totally confused and has no idea what she is supposed to be taking. Upon examination of her inpatient record you see that she was to stop her diltiazem due to severe constipation and begin Metoprolol which she was discharged on.
Patient case continued

• Upon inspection of her two pill planners you notice the Toprol XL and Diltiazem are both in her packs and she can’t really explain how she decides between the planners.

• What factors contributed to her polypharmacy?
Polypharmacy Definition

• Wide range of definitions
• No consensus definition
• Generally defined as “Administration of more medications than clinically indicated, representing unnecessary drug use.”
• Four or more medications used by many

Pharmacokinetic Changes in 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 continued

• Protein binding changes
  – Malnutrition
  – Dentures
  – Food preparation differences
  – Dietary restrictions

• Substance abuse affecting metabolism
  – Up to 10% of elderly use significant alcohol

Growth of Elderly Population

- Represent nearly 42 million
  - 13.3% of total population
- Have 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

http://www.aoa.gov/Aging_Statistics/Profile/2012/2.aspx
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

Polypharmacy in the Elderly

• Prevalence taking 5 or more medications around 7%

• Generally occurs due to three primary reasons:
  – Demographic Factors
  – Health Factors
  – Access to Healthcare

Don’t Forget OTC Meds

• Elderly Purchase 40% of OTCs
• Use of OTCs is 3-fold higher in elderly
• Nearly 15 billion spent each year on herbal products total
  – Elderly use twice as much herbals

Polypharmacy = Negative Outcomes

- Adverse Drug Events
- Poor Adherence
- Geriatric “Syndromes”
  - Urinary Incontinence
  - Cognitive Impairment
  - Loss of balance leading to falls/fractures

Adverse Drug Events

- WHO: “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 Events

• Risk is 15% with two medications
• Risk increases to 58% with 5 meds
• Risk increases to 82% with ≥ 7 meds
• Additional medications lead to greater incidence of drug interactions

Adverse Drug Events and the Elderly-Morbidity

- Nearly 17% of hospital admissions due to ADE
- Rate increases to 33% in patients ≥ 75 years old
- While in hospital, 17% of elderly experience an ADE

Adverse Drug Events in Older Adults: How to Avoid Them

What is an adverse drug event?
It is an unintended and unwanted effect that happens after taking a normal dose of a medicine.

Why are they more common in older adults?
Medicines have not been studied as much in older adults. The risks and benefits of medicines can vary, because getting older and getting sick affect people differently. There is less room for error, because older adults’ bodies do not adapt or repair themselves as easily.

Why do they happen?
They can happen from taking too many medicines or when several different medicines interact with each other. They can also happen because of changes in the kidneys and liver that occur as you age, and because of problems with adequate nutrition. Poor fluid balance, including either too much or too little fluids, can be a factor. Sometimes, a new condition or illness can cause adverse drug events.

How do I know if I am having one?
If you have new symptoms that you did not have before you started a new medicine or changed the dose of a medicine you have been taking, you may be having an adverse drug event. Tell your doctor if you have any new symptoms.

What will my doctor do if I have one?
Your doctor may have you stop taking a certain medicine, lower the dose of a medicine, or have you take a different one. Try to have one doctor, such as your family doctor, review all of your medicines, even ones prescribed by other doctors.

Where can I get more information?
Your doctor
AAFP’s Patient Education Resource
http://familydoctor.org
American Geriatrics Society
http://www.americangeriatrics.org
Consumer Reports Best Buy Drugs (reviews by drug, condition, and category)
http://www.consumerreports.org/health/best-buys/drugs/index.htm
Health in Aging
http://www.healthinaging.org

March 2013

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Guideline Contribution to Polypharmacy?

- Compliance often leads to multiple medications for many diseases
- Many times appropriate
- Perpetual assessment for each drug is required to limit inappropriate polypharmacy
- Right Drug-Right Circumstance-Right Disease=Highly individualized Care

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
- START Criteria
Beers Criteria

- Most commonly used tool
- Available at http://www.americangeriatrics.org
- App available for $2.99 at Itunes
- Two “avoidable” lists
  - One independent of diagnosis
- One “caution” list
- Newest additions in 2012
  - Megestrol acetate
  - Glyburide
  - Sliding scale insulin

American Geriatrics Society
2012 Beers Criteria Update
2012;60(4):616-631.
Selected Beers Medications

• Anticholinergics except amitriptyline
• Antipsychotics
• Benzos (especially long-acting)
• Indomethacin and Ketorolac
• Nitrofurantoin
• Digoxin > 0.125mg daily
• Spironolactone > 25mg daily

Selected Beers Medications

- Nonbenzodiazepine Hypnotics
  - > 90 days use
- NSAIDS in most circumstances
  - Require PPIs to be coadministered
  - Ketorolac and Indomethacin
- Meperidine
- Mineral Oil

American Geriatrics Society
2012 Beers Criteria Update
STOPP Criteria

- Screening Tool of Older Persons’ Potentially Inappropriate Prescriptions
- Comprised of 65 clinical criteria
- More common avoidable practices
- Some overlap with Beers criteria
- Not comprehensive

# STOPP Criteria

<table>
<thead>
<tr>
<th>Physiological System</th>
<th>Number of criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular system</td>
<td>17</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>13</td>
</tr>
<tr>
<td>Gastro-intestinal system</td>
<td>5</td>
</tr>
<tr>
<td>Musculoskeletal system</td>
<td>8</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>3</td>
</tr>
<tr>
<td>Urogenital system</td>
<td>6</td>
</tr>
<tr>
<td>Endocrine system</td>
<td>4</td>
</tr>
<tr>
<td>Drugs that adversely affect fallers</td>
<td>5</td>
</tr>
<tr>
<td>Analgesics</td>
<td>3</td>
</tr>
<tr>
<td>Duplicate drug classes</td>
<td>1</td>
</tr>
</tbody>
</table>
STOPP: Screening Tool of Older People’s Potentially Inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

Cardiovascular System

1. Digoxin at a long-term dose > 125 µg/day with impaired renal function
2. Loop diuretic for dependent ankle oedema only i.e. no clinical signs of heart failure
3. Loop diuretic as first-line monotherapy for hypertension
4. Thiazide diuretic with a history of gout
5. Non cardioselective Beta-blocker with Chronic Obstructive Pulmonary Disease
6. Beta-blocker in combination with verapamil
7. Use of diltiazem or verapamil with NYHA Class III or IV heart failure
8. Calcium channel blockers with chronic constipation
9. Use of aspirin and warfarin in combination without histamine H₂ receptor antagonist
10. Dipyridamole as monotherapy for cardiovascular secondary prevention
11. Aspirin with a past history of peptic ulcer disease without histamine H₂ receptor antagonist or Proton Pump Inhibitor
12. Aspirin at dose > 150 mg day
13. Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event
14. Aspirin to treat dizziness not clearly attributable to cerebrovascular disease
15. Warfarin for first, uncomplicated deep venous thrombosis for longer than 6 months duration
16. Warfarin for first uncomplicated pulmonary embolus for longer than 12 months duration
17. Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder
STOPP: Screening Tool of Older People’s Potentially Inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

Central Nervous System and Psychotropic Drugs.
1. Tricyclic antidepressants (TCAs) with dementia
2. TCAs with glaucoma
3. TCAs with cardiac conductive abnormalities
4. TCAs with constipation
5. TCAs with an opiate or calcium channel blocker
6. TCAs with prostatism or prior history of urinary retention
7. Long-term (i.e. > 1 month), long-acting benzodiazepines and benzodiazepines with long-acting metabolites
8. Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics
9. Long-term neuroleptics (> 1 month) in those with parkinsonism
10. Phenothiazines in patients with epilepsy
11. Anticholinergics to treat extra-pyramidal side-effects of neuroleptic medications
12. Selective serotonin re-uptake inhibitors (SSRIs) with a history of clinically significant hyponatraemia
13. Prolonged use (> 1 week) of first generation antihistamines i.e. diphenhydramine, chlorpheniramine, cyclizine, promethazine
STOPP: Screening Tool of Older People’s Potentially Inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

**Drugs that adversely affect fallers.**

1. Benzodiazepines
2. Neuroleptic drugs
3. First generation antihistamines
4. Vasodilator drugs with persistent postural hypotension i.e. recurrent > 20mmHg drop in systolic blood pressure
5. Long-term opiates in those with recurrent falls

**Analgesic Drugs**

1. Use of long-term powerful opiates e.g. morphine or fentanyl as first line therapy for mild-moderate pain
2. Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives
3. Long-term opiates in those with dementia unless indicted for palliative care or management of moderate/severe chronic pain syndrome

**Duplicate Drug Classes**

Any duplicate drug class prescription e.g. two concurrent opiates, NSAID’s, SSRI’s, loop diuretics, ACE inhibitors
START Criteria

- **Screening Tool to Alert Doctors To Right Treatments**
- Used in conjunction with STOPP criteria
- Identify correct treatments for elderly patients
- Composed of 22 criteria

START: Screening Tool to Alert doctors to Right Treatments

These medications should be considered for people ≥ 65 years of age with the following conditions, where no contraindication to prescription exists.

**Cardiovascular System**
1. Warfarin in the presence of chronic atrial fibrillation.
2. Aspirin in the presence of chronic atrial fibrillation, where warfarin is contraindicated, but not aspirin.
3. Aspirin or clopidogrel with a documented history of atherosclerotic coronary, cerebral or peripheral vascular disease in patients with sinus rhythm.
4. Antihypertensive therapy where systolic blood pressure consistently >160 mmHg
5. Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, where the patient’s functional status remains independent for activities of daily living and life expectancy is greater than 5 years.
6. Angiotensin Converting Enzyme (ACE) inhibitor with chronic heart failure
7. ACE inhibitor following acute myocardial infarction
8. Beta-blocker with chronic stable angina

**Respiratory System**
1. Regular inhaled β₂ agonist or anticholinergic agent for mild to moderate asthma or COPD
2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where predicted FEV1 <50%.
3. Home continuous oxygen with documented chronic type 1 respiratory failure or type 2 respiratory failure.

**Central Nervous System**
1. L-DOPA in idiopathic Parkinson’s disease with definite functional impairment and resultant disability
2. Antidepressant drug in the presence of moderate-severe depressive symptoms lasting at least three months.
Beers vs. STOPP

- 600 patients screened using either criteria
- Teaching hospital over 4-month period
- ADEs recorded and verified by expert panel for causality or contributory
- STOPP Criteria associated with avoidable ADEs leading to hospitalization ($p<0.001$)
- Beers Criteria NOT associated with reduction ($p=0.11$)

Next Step

• Incorporation of Criteria electronically
  – POE systems
  – Outpatient Pharmacy Records
  – PCMH models

• Need greater sensitivity
  – Identify greatest potential for ADEs

• Need greater specificity
  – “Alert fatigue” leading to ignoring potentially important ADEs

Schnipper JL. Ann Intern Med 2011;171:1019-20
Data for Interventions Helping Polypharmacy?

- Cochrane review identified 139 studies
- 10 studies made inclusion criteria
- Over 21,000 patients on at least 4 chronic medications
- Median age of 74 years old on 8 medications
- Type of intervention: 9 primarily pharmacist complex interventional; 1 decision support

Data for Interventions Helping Polypharmacy

- **Primary outcomes**
  - Appropriateness of meds prescribed by scoring system (MAI or Beers)
  - Hospital admissions

- **Secondary outcomes**
  - Adherence
  - ADRs, medication errors, drug-drug interactions
  - Quality of life

Outcomes

• Primary outcome
  – Number of inappropriate medications decreased by MAI score and Beers criteria but only significant for MAI scores
    • Significant heterogeneity between groups
  – Hospital admissions no difference between groups
    • Only 4 studies looked at this outcome

Outcomes

• Secondary outcomes
  – ADRs decreased (p=0.05)
  – Med errors unchanged
  – Data for drug interactions poor
  – Adherence not different (only one study)
  – Quality of life not different

Conclusion

• Pharmacist intervention had significant impact on polypharmacy prescribing
• Decision support limited
• Hard outcomes data limited
• Longevity of interventions?
• Prospective audit and feedback needed
• More studies examining hospitalizations effect from interventions required
Low-Hanging Fruit

- CDC estimates ADEs cause over 177,000 ED visits in United States
- Drugs on Beers List < 10%
- 33% of visits due to one of the following:
  - Warfarin
  - Insulin
  - Digoxin

Warfarin-Reasons for ADE

- Dietary indiscretion
- High patient variability
- Loading doses
- Multiple drug interactions
  - Antibiotics (FQ, Bactrim, Macrolides, Rifampin, Fluconazole, Metronidazole)
  - Anticonvulsants
  - Amiodarone (Reduce warfarin 25-50%)

Ageno W et al. CHEST 2012;141:e44S-88S.
**Warfarin Pearls**

- Restrict aspirin to 81mg daily
- Consistently reassess need for warfarin with CHA$_2$DS$_2$-VASc and HAS-BLED
- Novel anticoagulant switch in nonvalvular Afib and DVT/PE patients
  - Rivaroxaban for DVT/PE
  - Any of three potentially for nonvalvular Afib
- “Weight Watchers” approach
Insulin

- 95% of ED visits due to hypoglycemia
- 24% resulted in LOC or seizure
- 25.1% required hospitalization
### Table 2. Some Insulin Products

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
<th>Pregnancy Category</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin aspart – NovoLog (Novo Nordisk)</td>
<td>10 ml vial, 3 ml cartridge, 3 ml FlexPen</td>
<td>10-30 min</td>
<td>30 min-3 hrs</td>
<td>3-5 hrs</td>
</tr>
<tr>
<td>Insulin lispro – Humalog (Lilly)</td>
<td>10 ml vial, 3 ml cartridge, 3 ml KwikPen</td>
<td>30-60 min</td>
<td>2½-5 hrs</td>
<td>4-12 hrs</td>
</tr>
<tr>
<td>Insulin glargine – Apenira (Sanofi-Aventis)</td>
<td>10 ml vial, 3 ml cartridge, 3 ml SoloStar</td>
<td>1-2 hrs</td>
<td>4-8 hrs</td>
<td>10-20 hrs</td>
</tr>
<tr>
<td><strong>Regular Insulin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Humulin R (Lilly)</td>
<td>10 ml vial</td>
<td>30-60 min</td>
<td>2½-5 hrs</td>
<td>4-12 hrs</td>
</tr>
<tr>
<td>Novolin R (Novo Nordisk)</td>
<td>10 ml vial, 3 ml PenFill cartridge, 3 ml Innolet</td>
<td>1-2 hrs</td>
<td>4-8 hrs</td>
<td>10-20 hrs</td>
</tr>
<tr>
<td><strong>Intermediate-Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NPH</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Humulin N (Lilly)</td>
<td>10 ml vial, 3 ml PenFill cartridge, 3 ml Innolet</td>
<td>1-2 hrs</td>
<td>4-8 hrs</td>
<td>10-20 hrs</td>
</tr>
<tr>
<td>Novolin N (NovoNordisk)</td>
<td>10 ml vial, 3 ml PenFill cartridge, 3 ml Innolet</td>
<td>1-2 hrs</td>
<td>4-8 hrs</td>
<td>10-20 hrs</td>
</tr>
<tr>
<td><strong>Long-Acting</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Insulin detemir – Levemir (Novo Nordisk)</td>
<td>10 ml vial, 3 ml cartridge, 3 ml FlexPen, 3 ml Innolet</td>
<td>1-4 hrs</td>
<td>relatively flat</td>
<td>12-20 hrs</td>
</tr>
<tr>
<td>Insulin glargine – Lantus (Sanofi-Aventis)</td>
<td>10 ml vial, 3 ml cartridge, 3 ml SoloStar disposable device</td>
<td>1-4 hrs</td>
<td>no peak</td>
<td>22-24 hrs</td>
</tr>
<tr>
<td><strong>Pre-Mixed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novolin 70/30 (Novo Nordisk) (70% NPH, human insulin isophane suspen and 30% regular human insulin injection)</td>
<td>10 ml vial, 3 ml PenFill cartridge, 3 ml Innolet</td>
<td>30-60 min</td>
<td>2-12 hrs</td>
<td>18-24 hrs</td>
</tr>
<tr>
<td>Novolog Mix 70/30 (Novo Nordisk) (70% insulin aspart protamine suspen and 30% insulin aspart injection)</td>
<td>10 ml vial, 3 mL FlexPen</td>
<td>10-20 min</td>
<td>1-4 hrs</td>
<td>18-24 hrs</td>
</tr>
<tr>
<td>Humalog Mix 75/25 (Lilly) (75% insulin lispro protamine suspen and 25% insulin lispro injection)</td>
<td>10 ml vial, 3 ml Pen, 3 ml KwikPen</td>
<td>10-30 min</td>
<td>1-6½ hrs</td>
<td>14-24 hrs</td>
</tr>
</tbody>
</table>

1. Cartridges are used with pen injectors.
2. FDA pregnancy categories: B = no evidence or risk in humans; C = risk cannot be ruled out.
3. Profied, disposable syringe.
4. For use with OpTeren device.
5. Also available in a concentrated formula with 500 units per mL.
6. For use with NovoPen 4 or NovoPen Jr.
Reasons for Hypoglycemia

- Decreased intake of carbohydrates
- Increased exercise
- Weight Loss
- Bariatric Surgery
- Polypharmacy
Insulin Pearls

• Start low and go slow in new insulin patients
• Hypoglycemia increases mortality in several populations
• Hemoglobin A1c goals not < 7% for all
• American Geriatric Society recommends < 8% for:
  – Frail older adults
  – Life expectancy ≤ 5 years

Digoxin

- 80% of ED visits due to digoxin require hospitalization
- Over half involved doses > 0.125mg daily
- Does not decrease mortality in systolic heart failure
- Renally excreted
Digoxin-Pearls

• Use with caution in atrial fibrillation patients
• Sampling errors (get troughs only)
• Stick with doses of 0.125mg once daily
• Try to avoid in CKD patients
  – If required do q2-3 day dosing
Pearls for Decreasing Polypharmacy

- Start low and go slow
- Don’t set it and forget it (PK)
- Don’t leave home with it
- Ask about herbs, roots, nuts, berries
- Trust but verify
- Avoid narrow therapeutic index meds

Pearls for Decreasing Polypharmacy

• Review medication lists regularly
• Avoid too many changes at one time
• Begin with the end in mind
• Utilize Beers or START criteria for regular assessment

Pretorius RW et al. *Am Fam Physician.* 2013;87:331-6
Conclusion

• Polypharmacy represents a significant cause of morbidity in the elderly
• Data showing significant effects on these “hard” outcomes is limited
• STOPP and Beers criteria available for screening
• Special focus on warfarin, insulin, and digoxin