Geriatric Medication Safety
A Focus on Appropriate Medication Selection
Katherine M. Juba, PharmD, BCPS

Learning Objectives

- Differentiate between an adverse drug reaction (ADR) and an adverse drug event (ADE).
- Identify ADE risk factors in older adults.
- Apply strategies to ensure safe medication use in older adults.
- Utilize clinical tools to recognize potential drug-related problems in older adults.
- Identify limitations when applying the START, STOPP, and Beers Criteria in patient care.
- Discuss limitations of herbal and supplement use in older adults.

Definitions

- **Adverse drug reaction (ADR)**
  - A specific reaction usually related to a medication’s pharmacology

- **Adverse drug event (ADE)**
  - Injury due to a medication
  - May include ADR and events related to medication use

- **Medication error**
  - Inappropriate medication use that may or may not result in harm

You deliver that bag of fentanyl for CC, a 76 yo female in the Surgical ICU. The nurse starts the infusion. Thirty minutes later, CC is found unresponsive, her BP is reading 72/45, HR of 67. The head nurse come to the room and found that the fentanyl drip is connected to CC’s epidural catheter instead of her PICC line.

Is this an ADR and/or an ADE?

Difficulty to estimate ADE prevalence in older adult population

- Emergency Department visits: 5.9% to 12.6%\(^{1-3}\)
  - Older adults more likely to be hospitalized than younger patients
- Community dwelling: 5.5% to 33%\(^{4-5}\)

Impact healthcare costs and hospital admission rates

Difficult to estimate ADE prevalence in older adult population

- Emergency Department visits: 5.9% to 12.6%\(^{1-3}\)
  - Older adults more likely to be hospitalized than younger patients
- Community dwelling: 5.5% to 33%\(^{4-5}\)

Impact healthcare costs and hospital admission rates

### ADE - Risk Factors

- Increasing age
- Female gender
- Hx prior ADR
- Prolonged hospitalization
- Fragmented medical care
- Multiple disease states/poor health status
- Polypharmacy

### Where ADEs Occur

- Prescribing/Medication Selection
- Dispensing
- Administration/Adherence
- Monitoring

### Prescribing

- Medication without an indication
- Indication without a medication
- Duplicate medications
- Wrong drug
- Wrong dose
- Wrong route or formulation
- Wrong time or frequency
- Wrong duration
- Drug interactions
- Allergies, contraindications

Tools to Evaluate Potentially Inappropriate Medication (PIM) Prescribing

PIM Prescribing Tools

- Zhan Criteria (2000)
- START/STOPP Criteria (2008)
- French Consensus Panel List (2007)
- Norwegian General Practice Criteria (2009)

Patient Case

- DD is an 88 y.o. female patient who presents to the geriatric clinic with her daughter. The patient is orientated to self and place. She is able to answer simple commands. The patient c/o left leg pain only.
- You are asked to evaluate the patient’s medications prior to her visit with the medication provider.
### Social Hx:
Widowed; patient moved in with her daughter 3 yrs three years ago secondary to difficulty with ADLs at home

### MMSE:
18/30 (1 month ago)

### PMH:
Dementia, CHF, Hx Colon CA, COPD, Anxiety, and HTN

### Labs:
- BUN: 31 mg/dL
- SCr: 1.7mg/dl
- Alb: 2.9 g/dl
- GFR: 29 ml/min/1.72m²
- BG: 84mg/dl
- Electrolytes WNL
- LFTs WNL

### Vital Signs:
- HR: 82 bpm
- RR: 22 breaths/min
- O₂ Sat: 96% on RA
- BP: 132/70 mmHg
- Temp: 98.6°F
- Ht: 5’4”, Wt: 95 lbs

### Current Medications

<table>
<thead>
<tr>
<th>Current Medications</th>
<th>Allergies: Codeine</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA 81mg PO Daily</td>
<td></td>
</tr>
<tr>
<td>Lorazepam 1mg PO Q6h</td>
<td></td>
</tr>
<tr>
<td>Lorazepam 0.5mg PO Q4h prn anxiety (2 doses/day)</td>
<td>Oxycodeone/Acetaminophen 5/325mg PO Q4h prn BTP (4 doses/day)</td>
</tr>
<tr>
<td>Miralax Mix 17g in 8 oz water and drink Daily</td>
<td>Estradiol 0.5mg PO Daily</td>
</tr>
<tr>
<td>Lactulose 100/15ml PO Daily</td>
<td>Flonase 1 spray in each nostril BID</td>
</tr>
<tr>
<td>HCTZ 25mg PO Daily</td>
<td>MVI 1 tab PO Daily</td>
</tr>
<tr>
<td>Lisinopril 10mg PO Daily</td>
<td>Prevacid 30mg PO Daily</td>
</tr>
<tr>
<td>Megestrol Susp 400mg PO BID</td>
<td>Ginkgo Biloba 160mg (2tabes) PO</td>
</tr>
<tr>
<td>Metazepine 35mg PO QHS</td>
<td></td>
</tr>
</tbody>
</table>
Most commonly used criteria on “drugs to avoid” in older adults
- Center for Medicare Services (CMS) mandated for nursing home
- Developed for use in community dwelling and nursing home patients
- Recommendations compiled by geriatric panel
  - Review of medical literature
  - Expert opinion

Inappropriate medications for all elderly patients
- Drugs that should not be prescribed above criteria doses
- Drug-drug and drug-disease combinations to avoid
- Distinguishes between high and low severity

Common Examples of Drugs to Avoid per Beers’ Criteria
- Cyclobenzaprine
- Carisoprodol
- Amitriptyline
- Doxepin
- Dicyclomine
- Hydroxyzine
- Promethazine
- Fluoxetine
- Diazepam
- Amphetamines
- Naproxen
- Indomethacin
- Amiodarone
- Nitrofurantoin
- Doxazosin
- Clonidine
Drugs that should not be prescribed above criteria dose in the older adult

- Lorazepam (3 mg/day)
- Alprazolam (2 mg/day)
- Temazepam (15 mg/day)
- Digoxin (>125 mcg/day)
  - Except when treating atrial arrhythmias

Arch Intern Med 2003;163:2716-2724.

Not an all inclusive drug list
Not updated to reflect changes in clinical practice since 2002
- Darvon®, Darvocet® removed from market
- NSAIDs and Cardiovascular AEs
  - Increased risk of death in elderly patients taking atypical antipsychotics
- Evidence of validity is inconclusive
  - Impact on mortality and cost

HOWEVER.... It is a reasonable starting place

According to the Beers’ Criteria, is DD taking any potentially inappropriate medications?

What are the medications’ severity ratings?
Screening Tool to Alert Doctors to the Right Treatment

Most medical literature focuses on inappropriate prescribing in older adults
- Lack of evidence about medication omissions

START criteria
- Evidence-based screening tool to alert prescribers to medications that are not prescribed but indicated
- Based on body system
- Developed by academic geriatrician with expert panel review

Age and Aging. 2007;36:632-638.

---

**START Criteria**

**Endocrine System**
- (i) Metformin with type 2 diabetes +/- Metabolic Syndrome (in the absence of renal impairment present (i.e. blood urea >33.6 mg/dL, ± serum creatinine >2.3 mg/dL).
- (ii) ACE inhibitor or Angiotension Receptor Blocker in diabetes with nephropathy i.e. overt dipstick proteinuria or microalbuminuria (>30 mg/24 h) ± serum biochemical renal impairment (blood urea >3.4 mg/dL or serum creatinine >1.7 mg/dL).
- (iii) ASA therapy in diabetes mellitus with well controlled BP
- (iv) Statin therapy in diabetes mellitus if fasting serum cholesterol >193 mg/dL or additional cardiovascular risk factor(s) present.

---

**START Criteria**

**Central Nervous System**
- (i) L-DOPA in idiopathic Parkinson’s disease with definite functional impairment and resultant disability.
- (ii) Antidepressant in the presence of clear-cut depressive symptoms, lasting at least 3 months.

**Locomotor System**
- (i) Disease-modifying anti-rheumatic drug (DMARD) with known, moderate–severe rheumatoid disease lasting more than 12 wks
- (ii) Bisphosphonate in patients taking glucocorticoids for more than 3 months (i.e. chronic corticosteroid therapy).
- (iii) Calcium and vitamin D supplement in patients with known osteoporosis (previous fragility fracture, acquired dorsal kyphosis).
### START Criteria Limitations

- Lack of supporting data on primary and secondary prevention outcomes
- Cost impact for medication omissions
  - New costs for secondary prevention
- Lack of validation of findings in clinical practice
- Does not provide for individualization 2nd to shifting on goals of care
  - Limited life expectancy
  - Palliation versus secondary prevention

### Patient Case

- According to the START criteria, are there additional medications that DD should receive?

### STOPP Criteria

- **Screening Tool of Older Persons’ Potentially Inappropriate Prescriptions**
- Evidence-based tool to address *clinically significant criteria for potentially inappropriate prescribing*
  - Goal: improving limitations of other tools and reflect clinical practice changes
- Same research group that developed START criteria
  - Expert geriatric panel review
  - Based on body system

STOPP Criteria

1. Omeprazole, pantoprazole or other PPIs for treatment of diarrhea of unknown cause (risk of delayed diagnosis, may exacerbate constipation with overuse; diarrhea, may precipitate toxic megacolon in inflammatory bowel disease, may delay recovery in unresolved gastritis) [Lebenthal et al. 1987, Theilen and Guarrardi 2004].

2. Clopidogrel in the elderly (overdosing possible) [Vincent et al. 1986, Theilen and Guarrardi 2004].

3. Selective serotonin re-uptake inhibitors (SSRIs) with a history of clinically significant hypotension or serious hypotension (hypotension < 100 mmHg within the previous 2 months) [Karch and Spirito 2005].

4. Anticholinergic antidepressants for chronic constipation (risk of exacerbation of constipation) [Bose and et al. 2004].

A. Cardiovacular system

1. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

2. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

3. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

4. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

5. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

6. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

7. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

8. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

9. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

10. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

11. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

12. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].

13. Calcium channel blockers with chronic constipation (may exacerbate constipation) [Douglas and Sorkin 2004].
STOOPP Criteria

E. Gastrointestinal
1. Nonsteroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent (uspiramine) + aspirin (primary risk of peptic ulcer disease) (Kupper et al. 2004).
2. NSAID with moderate to severe hypertension (risk of exacerbation of hypertension) (Mehlum 2000).
3. NSAID with heart failure (risk of exacerbation of heart failure) (Sircar and Szafir 2005).
4. Long-term use of NSAID (> 3 months) for symptom relief of mild osteoarthritis (simple analgesics preferred and usually as effective for pain relief) (Pikarsky et al. 2000).
5. Alcellin and NSAID together (risk of gastrointestinal bleeding) (Kallstrom et al. 2006).
6. NSAID with chronic renal failure (risk of excretion of fluid retention) (Cheng and Yamanaka 2006).
8. Long-term NSAID or corticosteroids for chronic treatment of gout where there is no contraindication to allopurinol (basketproof when choice propylthiophosphate in gout) (Becherger 2004, Turbill 2004).

F. Urinary System
1. Regular antihypertensive drugs with dementia (risk of increased conduction agglutination) (May et al. 2008, Stavros 2000).
2. Antihypertensive drugs with chronic glomerulonephritis or chronic renal insufficiency (Stavros 2000).
3. Antihypertensive drugs with chronic constipation (risk of exacerbation of constipation) (Stavros 2000).
4. Antihypertensive drugs with chronic renal failure (risk of fluid and electrolyte retention) (Stavros 2000).
5. u-Alkalies in patients with chronic or recurrent episode (risk of urinary frequency and incontinence) (Kesler and Doolin 2000).
6. u-Alkalies with long-term urinary catheter (e.g., more than 2 months drug not included).

STOOPP Criteria

G. Endocrine System
1. Glucorticoid or chemo-therapy with type 2 diabetes mellitus (risk of prolonged hypoglycemia) (Chellah and Barge 2004).
2. u-Alkalies in those with diabetes mellitus and frequent hypoglycemic episodes i.e. > 1 episode per month (risk of exacerbation of hypoglycemia) (Chellah and Barge 2004).

H. Drugs that adversely affect falls
1. Thiazolidinediones (oral agents, may cause reduced vision, impairment balance) (Tieni 2003).
2. Neurontic drugs (may cause polynephritis, papillary necrosis) (Tieni 2003).
3. First-generation antihistamines (prolongation, may impair awareness) (Butler et al. 2002).
4. Vasodilator drugs with persistent postural hypotension i.e. recurrent > 20 mmHg drop in systolic blood pressure (risk of syncopal falls) (Leong et al. 1999).

STOOPP Criteria

I. Anxiolytic Drugs
1. Use of long-term powerful opiates (e.g., morphine or fentanyl) as first-line therapy for mild-to-moderate pain (World Health Organization analgesic ladder not observed) (American Geriatrics Society Panel on Persistent Pain in Older Persons 2002).
2. Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives (risk of severe constipation) (Nash 1999).
3. Long-term opiates in those with dementia unless indicated for palliative care or management of moderate/severe chronic pain syndrome (risk of exacerbation of cognitive impairment) (American Geriatrics Society Panel on Persistent Pain in Older Persons 2002).

J. Other drug classes
Any duplicate drug class prescription, e.g., two concurrent opiates, NSAIDs, SSRIs, loop diuretics, ACE inhibitors (optimization of monotherapy within a single drug class should be observed prior to considering a new class of drug).
**STOPT Criteria Limitations**

- Lack of validation of findings in clinical practice
  - Lack of outcomes data
    - Cost
    - Clinical efficacy
- Balance between limitations in START criteria (omission) with STOPP criteria (inappropriate prescribing)

---

**Patient Case**

- According to the STOPP criteria, is DD receiving any potentially inappropriate medications?

---

**Beers’ Versus STOPP Criteria**

Prospective study comparing the performance of STOPP and Beers’ criteria in detecting PIMs and related ADEs in older patients admitted to the hospital via ED

- 715 consecutive acutely ill, older adults in the emergency department
- Study investigators determined if PIMs contributed to or caused admission
- ADE was the cause or contributory factor for admission in 90 pts. (12.5% of all admissions)

Age and Aging 2008;37(6):673-79

Beers’ Versus STOPP Study

Most common presenting events:
- Falls, with following injuries:
  - fractures – 27%
  - Ischemic Heart Disease (IHD) – 12%
  - Respiratory Tract Infection – 10%
  - Stroke – 7%
  - Cardiac failure – 6%
  - Delirium – 5%

Most prevalent co-morbidities:
- HTN (40%)  ■ IHD (29%)  ■ AFib (18%)
- Stroke (16%)  ■ DM (16%)  ■ Dementia (10%)

Beers’ Versus STOPP Criteria

- STOPP criteria results
  - 336 PIMs (in 247 pts.) detected (from total of 715 pts.)
    - 82 patients (or 27%) with PIMs presented an associated ADE (11.5% of total admissions)
- Beer’s criteria results
  - 226 PIMs (in 177 pts.) detected (from total of in 715 pts)
    - 43 patients with PIMs presented an associated ADE (6% of total admissions)

P<0.001
Includes OTC medications, herbals, and supplements

Community dwelling patients often utilize these products without appropriate assessment and monitoring by a healthcare provider

Use of herbals and dietary supplements has doubled among geriatric patients since 2000

Self-care with herbals, OTC medications, and supplements may contribute to
- Medications without an indication
- Duplicate therapy
- Drug-interactions

Use of dietary supplements in Older Adults

PIMs found in Common OTCs

Alternative Therapies

1. Beers’s Criteria
   - Diphenhydramine
   - Chlorpheniramine
   - Bisacodyl
     - Except with chronic opioid use
   - Mineral oil
   - Cimetidine
   - Naproxen sodium

2. STOPP Criteria
   - ASA
   - 1st Generation Antihistamines
     - Diphenhydramine, Chlorpheniramine
   - NSAIDs
     - Ibuprofen, Naproxen
   - Loperamide
   - PPIs
     - Lansoprazole, Omeprazole, Prevacid, Zentel

3. Treatment that is not within standard evidence-based medical practice
4. Used instead of conventional medicine
   - eg. breast CA patient who decides to utilize herbals instead of chemotherapy
5. Intended to treat a disease state or improve organ function

Complementary Therapies

“Alternative” therapies are used in combination with conventional medical practices
- eg. massage therapy in cancer patients receiving chemotherapy
- eg. Coenzyme Q10 use in patients taking warfarin
  - Coenzyme Q10 improves cardiovascular disease?
  - Decreased warfarin efficacy

Herbal and Supplement Use

First Limitation:
- Unregulated

Acute Selenium Poisoning

- Combination dietary supplement product
  - 227 cases of selenium poisoning in 9 states
- Tested product selenium content: 40,800 µg/1 oz
- Labeled selenium content: 200 µg/1 oz
  - RDA: 55 µg/day

Reported Symptoms of Selenium Toxicity After Consuming a Misformulated Dietary Supplement

Table 1. Reported Symptoms of Selenium Toxicity After Consuming a Misformulated Dietary Supplement

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>156 (70)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>144 (70)</td>
</tr>
<tr>
<td>Headache</td>
<td>140 (70)</td>
</tr>
<tr>
<td>Joint pain</td>
<td>135 (67)</td>
</tr>
<tr>
<td>Nausea</td>
<td>133 (65)</td>
</tr>
<tr>
<td>Headache</td>
<td>115 (57)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>59 (28)</td>
</tr>
<tr>
<td>Fever</td>
<td>45 (21)</td>
</tr>
<tr>
<td>Rash</td>
<td>27 (12)</td>
</tr>
</tbody>
</table>


“Conclusions: Toxic concentrations of selenium in a liquid dietary supplement resulted in a widespread outbreak. Had the manufacturers been held to standards used in the pharmaceutical industry, it may have been prevented.”


Quality of Supplements??
- Quantity of products listed
- Contaminants
- Misidentification or Cost Savings?
  - 1997: woman hospitalized with irregular HR after taking what she thought was an herbal laxative.
  - Investigation: product contained *digitalis* instead of *plantain*. The supplier had misidentified the herb in its raw form (Washington Post 2006)
    - Plantain – laxative
    - Digitalis – antiarrhythmic
Herbal and Supplement Use

- Unregulated
- Limited / absent clinical data
- Efficacy
  - Drug-herbal, drug-supplement, or drug-lab interactions
    - Difficult to distinguish confounders in combination products
- Adverse effects incidence
  - Reporting
  - Impact of product variability
  - Dose and length of therapy
- Patient specific factors

St. John’s Wort Interactions

- St. John’s Wort (SJW) most clinical evidence
- CYP 1A2, 2C9, 2C19, 2D6, 2E1, 3A4
  - Many clinically significant drug-herbal interactions
- Warfarin
  - Increased metabolism via CYP3A4 induction
  - Decreased metabolism via CYP1A2 inhibition

Herbal and Supplement Use

- Difficult to recommend widespread supplement use
  - Exception calcium/vitamin D in osteoporosis
- Counsel patients on lack of evidence
  - Document conversation
- Discourage use of combination products
- Encourage use of standardized products

Evidence-Based Free Patient Websites

- Medline Plus
  - US National Library of Medicine and National Institutes of Health (NIH)
- Memorial Sloan Kettering Cancer Center

Look for these seals …

- U.S. Pharmacopeia Dietary Supplement Verification Program – USP
- [http://www.consumerlab.com](http://www.consumerlab.com)
Patient Case

- Utilizing your clinical judgment
- What additional information would be beneficial?
- What additional interventions do you recommend?