Objectives

- Explain concepts of altered pharmacokinetics in the elderly
- Understand drug related problems in the elderly
- Discuss strategies for minimization of drug related problems in the elderly
- Utilize tools for identifying inappropriate & appropriate medications in the elderly
- Implement clinical decisions related to drug-related problems
Pharmacotherapy in the Elderly

- Geriatric: >65 years of age
  - 44-57% take 5-10 medications
  - 12-25% take ≥11 medications
- 30% of all medications dispensed to elderly
- Expenditures expected to increase with aging population
- Altered pharmacokinetic and pharmacodynamic principles
- Greater susceptibility to ADEs

Pharmacokinetics & Pharmacodynamics

**Pharmacokinetics**
- Effect of body on drug
- **ADME**
  - Absorption → Distribution → Metabolism → Excretion

**Pharmacodynamics**
- Effect of drug on body
- Medication exhibiting its pharmacologic effect
Geriatric Absorption

- Passive diffusion generally unaltered
- Active transport impaired
  - Decreased absorption of vitamin B12, iron, calcium, magnesium
  - Decreased first-pass effect in hepatic or gut wall

Geriatric Absorption

- GI disease states alter gastric pH and/or intestine motility
  - Medications may increase pH (PPI or H2RA)
- Physiologic changes & effects on routes of administration
  - Decreases in subcutaneous tissue, skin, muscle mass → subcutaneous, transdermal, and IM administration less predictable and should be avoided if possible
Geriatric Distribution

- Decreases in body mass & fluid content \(\rightarrow\) decreases in volume of distribution for hydrophilic drugs
- Decreases in blood flow/tissue perfusion \(\rightarrow\) decreases in distribution of drugs to organs
- Changes in protein binding (decreased albumin, minimal changes in glycoprotein) \(\rightarrow\) minimal changes for most drugs
- Blood brain barrier permeability increased \(\rightarrow\) brain subjected to higher levels of drugs & toxins

Geriatric Metabolism

- Decreased hepatic blood flow & decrease enzyme function \(\rightarrow\) decreased metabolism & elimination via phase I
  - Exception: highly albumin-bound drugs
- Decreases in albumin concentrations \(\rightarrow\) higher fraction of unbound drug \(\rightarrow\) higher amount of drug available for hepatic metabolism & total hepatic clearance increases
Geriatric Excretion

- Age-related reductions in GFR well documented
- Decline often linked to concurrent disease states common in elderly
  - Hypertension, heart disease, diabetes, etc.
- Important to calculate CrCl in older adults to ensure all medications are being dosed appropriately!
- Note: exceptions exist, some older adults will maintain adequate renal function

Altered Pharmacodynamics in Elderly

- General trend of increased “sensitivity” to drugs
  - Changes in concentrations of drug at receptor
  - Changes in receptor numbers & affinity
  - Post-receptor alterations
  - Impairment of homeostatic mechanisms
- Especially sensitive to CNS & cardiovascular effects!
  - Cardiovascular changes
  - Cross BBB more easily
  - Changes in neurotransmitters
  - Reductions in brain size & weight
Drug Related Problems

- **Polypharmacy**
  - 44-59% of geriatric outpatients take ≥1 unnecessary medication

- **Inappropriate Prescribing**
  - 25-42% of long term care residents take ≥1 medication with a dose, duration, duplication, or drug-interaction problem

- **Underuse**
  - Cohort study found 57% of patients had higher risk of cardiovascular events due to preventative medication underuse

- **Nonadherence**
  - Accounts for 4-11% of hospital admissions
  - Secondary to adverse effects, complex regimens, lack of understanding, functional difficulties, cost, etc.

Minimization of Drug Related Problems

- **Careful history taking**
  - Over the counter medications (nonprescription medications, dietary supplements, herbals)?
  - May be limited by patient’s cognition, sensory, lack of knowledge/medical records

- **Assessment of adherence & compliance**
  - Minimize multiple times per day dosing
  - Utilize pillboxes, aid from caregiver or family member, use of checklists and/or calendars
  - Provide patient with updated copy of medication list
Minimization of Drug Related Problems

- Therapy assessment for overuse
  - Does each drug have an indication?
  - Is each drug effective?
  - Is each drug safe?
  - Risks outweigh benefits?
  - Duplication?
- Therapy assessment for underuse
  - Is there an indication not being treated?
  - Preventative therapy?
- Monitoring therapy for efficacy and safety
  - Labs, vital signs, symptoms, drug-drug interactions, etc.

Tools

- 2015 Beers Criteria
- Screening tool to alert to right treatments (START) Version 2, 2014
- Screening tool of older people’s prescriptions (STOPP) Version 2, 2014
Beers Criteria

- Published by American Geriatric Society
- List of potentially inappropriate medications in older adults
  - Divided into 5 categories
- Widely used by geriatricians in clinical settings
- Originally published in 1997, revised multiple times, most recent in 2015
- Developed through expert consensus from literature review and questionnaire
- Used by CMS for nursing home regulation

2015 Beers Criteria Categories

- Potentially Inappropriate Medications (PIMS) in Older Adults
- PIMS in Older Adults due to Drug-disease Interactions that may Exacerbate the Disease or Syndrome
- Drugs to be Used with Caution in Older Adults
- Potentially Clinically Important Non-anti-infective Drug-drug Interactions that should be Avoided in Older Adults
- Potentially Clinically Important Non-anti-infective Drugs that Should be Avoided or Dose Reduced with Varying Levels of Kidney Function in Older Adults
Beers Criteria

- **Strengths**
  - Evidence based
  - Includes drug-drug interactions, drug-disease interactions, renal dosing
  - Updated multiple times since original publication
  - **Effective tool for informing clinicians on which medications to re-evaluate for appropriateness and/or avoid initially**

START/STOPP (Version 2)

- Published by British Geriatrics Society
- List of inappropriate medications & potential prescribing omissions
- Divided by organ system
- Addresses drug-disease interactions, drug-drug interactions, duration, doses based on eGFR
- Criteria developed through expert consensus from literature review
STOPP/START Categories

**STOPP**
- Indication
- Cardiovascular system
- Antiplatelet/anticoagulant drugs
- CNS & psychoactive drugs
- Renal System
- GI System
- Respiratory system
- Musculoskeletal system
- Urogenital system
- Endocrine system
- Drugs that increase falls
- Analgesics
- Antimuscarinic/anticholinergic

**START**
- Cardiovascular system
- Respiratory system
- CNS & eyes
- Gastrointestinal system
- Musculoskeletal system
- Endocrine System
- Urogenital system
- Analgesics

START/STOPP

- **Strengths**
  - Evidence based!
    - All STOPP criteria medications are significantly associated with ADE, unlike Beers
    - RCT demonstrated when applied within 72 hours of admission, ADR reduced by 9.3% (ARR), NNT 11, and decreased length of stay by 3 days
  - Updated
  - **Effective tool for informing clinicians on which medications to evaluate for appropriate use and/or to avoid initially AND which medications to start**
Limitations

**Beers**
- Does not address prescribing omissions, drugs without indication, vaccines
- Not well-separated by organ system
- Uses some medications less commonly prescribed
- RCTs have demonstrated a greater number of PIM reductions with START/STOPP*

**START/STOPP**
- Does not provide strength or quality
- eGFR instead of CrCl, limited renal dosing
- Limited inclusion of DI
- Does not separate by problem-type
- Rationale less detailed

**Does not address duplication or ALL problems**
- Older adults often under-represented in trials
- Search strategies may have missed unpublished reports
- Not applicable to hospice/palliative care
- Problems not prioritized
- **Does not replace clinical judgment!!!**

PIM Comparison

- **Beers only**
  - Aspirin*
  - Dabigatran*
  - Prasugrel*
  - Digoxin for a.fib and heart failure
  - Nitrofurantoin
  - Nifedipine IR
  - Barbital
  - Dronedarone
  - Megestrol
  - Growth hormone
  - Sliding scale insulin
  - Meperidine
  - Desmopressin
  - Medications that can cause insomnia

- **STOPP only**
  - Loop diuretics (first-line HTN)
  - Aspirin >160mg
  - Digoxin for heart failure
  - Elemental iron >200mg/day
  - COX-2 selective agents
  - Systemic corticosteroids for COPD
  - Non-selective beta-blockers
  - Transdermal opioids
  - Constipating medications
  - Opioid without laxative
  - Long-acting opioid without PRN
Application

An 80 year old female is new to your clinic. She is 5’2” and weights 120 lbs

PMHx:
- HTN
- CAD/MI 10 years ago
- Atrial fibrillation
- Diabetes
- Osteoporosis, Hx hip fracture
- GERD
- Osteoarthritis
- Constipation
- Insomnia
- Anxiety

Medications:
- Diltazem CD 240mg daily
- Digoxin 0.125mg three times weekly
- Warfarin 5mg daily
- Insulin glargine 30 units qhs
- Insulin lispro 5 units tid ac
- Ibuprofen 200mg TID
- Polyethylene glycol 17G daily
- Omeprazole 40mg daily
- Alendronate 70mg daily x 5 years
- Sertraline 50mg PO daily
- Diphenhydramine 50mg PRN sleep
- Clonazepam 1mg PO q12h

BEERS criteria application

<table>
<thead>
<tr>
<th>Medication</th>
<th>Rationale</th>
<th>Recommendation</th>
<th>Quality</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digoxin</td>
<td>a.Fib &amp;CHF : more effective alternatives, may be associated with increased mortality</td>
<td>Avoid</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Highly anticholinergic, clearance reduced, tolerance when used as a hypnotic</td>
<td>Avoid</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Increased sensitivity, decreased metabolism of long-acting agents, increased risk of cognitive impairment, delirium, falls fractures</td>
<td>Avoid</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
</tbody>
</table>
### Beers Criteria Application

#### PIMs

<table>
<thead>
<tr>
<th>Medication</th>
<th>Rationale</th>
<th>Recommendation</th>
<th>Quality</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proton-pump inhibitors</td>
<td>Risk of c diff, bone loss, fractures</td>
<td>Avoid &gt;8 weeks, unless high risk</td>
<td>High</td>
<td>Strong</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Risk of gastrointestinal bleeding, PUD, especially if on anticoagulant, antiplatelet agent, or IV corticosteroid. PPI reduces but does not eliminate risk. GI bleeds or ulcers occur in 1% treated for 3-6 months, and ~2-4% treated for 1 year, trends continue with longer durations</td>
<td>Avoid chronic use, unless other alternatives are not effective and patient can take gastroprotective agent</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
</tbody>
</table>

### Beers Criteria Application

#### Drug-Disease Interactions

<table>
<thead>
<tr>
<th>Disease</th>
<th>Medication(s)</th>
<th>Rationale</th>
<th>Recommendation</th>
<th>Quality</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of falls or fractures</td>
<td>Anticonvulsants, Antipsychotics, Benzodiazepines, Hypnotics, TCAs, SSRIs, Opioids</td>
<td>Ataxia, impaired psychomotor function, syncope, falls. Shorter acting benzodiazepine preferred. If needed, consider reducing other CNS-active medications to</td>
<td>Avoid</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
<tr>
<td>Dementia or cognitive impairment</td>
<td>Anticholinergics, Benzodiazepines, H2-receptor antagonists, Hypnotics, Antipsychotics</td>
<td>Adverse CNS effects associated with increased risk of CVA and mortality in patients with dementia</td>
<td>Avoid</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
</tbody>
</table>
### Beers Criteria Application

#### Drugs to Use with Caution

<table>
<thead>
<tr>
<th>Medication(s)</th>
<th>Rationale</th>
<th>Recommendation</th>
<th>Quality</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin for primary prevention of cardiac events</td>
<td>Lack of evidence vs benefit in adults aged ≥80</td>
<td>Use with caution</td>
<td>Low</td>
<td>Strong</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>May exacerbate or cause SIADH or hyponatremia, monitor sodium</td>
<td>Use with caution</td>
<td>Moderate</td>
<td>Strong</td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Mirtazepine</td>
<td></td>
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<td></td>
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<tr>
<td>SNRIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRIs</td>
<td></td>
<td></td>
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<tr>
<td>TCAs</td>
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</tbody>
</table>

### Beers Criteria Application

#### Drug-drug Interactions

<table>
<thead>
<tr>
<th>Drug or class</th>
<th>Interacting drug or class</th>
<th>Rationale</th>
<th>Recommendation</th>
<th>Quality</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants</td>
<td>≥2 other CNS-active drugs</td>
<td>Increased risk of falls and fractures</td>
<td>Avoid ≥3 CNS-active drugs, minimize use</td>
<td>Moderate</td>
<td>High</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypnotics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warfarin</td>
<td>NSAIDs</td>
<td>Increased risk of bleeding</td>
<td>Avoid when possible, monitor for bleeding</td>
<td>High</td>
<td>Strong</td>
</tr>
<tr>
<td></td>
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</tbody>
</table>
Beers Criteria Applications
Unaddressed problems?

- Drug-disease interactions
  - Omeprazole-osteoporosis
  - Alendronate-GERD
- Duration
  - Alendronate drug holiday >5 years
- Prescribing omissions
  - Calcium and vitamin D
  - Statin
  - ACE-I
  - Aspirin?
  - Vaccines?

STOPP Application

- Cardiovascular System
  - Digoxin for heart failure with normal systolic ventricular function (no clear evidence of benefit)
STOPP Application

- Antiplatelet/anticoagulant drugs
  - Antiplatelet agents with anticoagulant in patients with stable coronary, cerebrovascular, or peripheral arterial disease (no added benefit from dual therapy)
  - NSAID and anticoagulant (risk of major GI bleed)

STOPP Application

- Central Nervous System and Psychotropic Drugs
  - SSRI with current or recent significant hyponatremia i.e. serum NA+ <130mmol/L (risk of exacerbating or precipitating hyponatremia)
  - Benzodiazepines for >4 weeks (risk of prolonged sedation, confusion, impaired balance, falls; all should be withdrawn gradually if taken for more than 4 weeks as there is a risk of causing benzodiazepine withdrawal syndrome if stopped abruptly)
  - Anticholinergics in patients with delirium or dementia (Risk of exacerbation of cognitive impairment)
  - First-generation antihistamines (safer, less toxic antihistamines available)
STOPP Application

- Renal System
  - Digoxin at long-term dose greater than 0.125mg/day if eGFR < 30mL/min/1.73m (risk of digoxin toxicity)
  - NSAID’s if eGFR < 10mL/min/1.73m²

- Gastrointestinal System
  - PPI for uncomplicated peptic ulcer disease for >8 weeks (dose reduction or earlier discontinuation indicated)
  - Drugs likely to cause constipation (anticholinergics) in patients with chronic constipation where non-constipating alternatives exist
STOPP Application

- **Musculoskeletal System**
  - NSAID other than COX-2 selective agents with history of PUD or GI bleed, unless concurrent PPI or H2 antagonist (risk of peptic ulcer relapse)
  - NSAID with severe hypertension (risk of exacerbation)
  - Long-term use of NSAID (>3 months for osteoarthritis when APAP has not been trialed)
  - Cox-2 selective NSAID with concurrent cardiovascular disease
  - Oral bisphosphonate in patients with upper GI disease (risk of relapse/exacerbation)

- **Drugs that Predictably Increase Fall Risk**
  - Benzodiazepines (sedative, reduced senses, impaired balance)
  - Concomitant use of two or more drugs with antimuscarinic/anticholinergic properties
START Application

- Cardiovascular System
  - Antiplatelet therapy with a documented history of coronary, cerebral, or PVD
  - Statin therapy with documented history of coronary, cerebral, or peripheral vascular disease, unless patient’s status is end-of-life or >85 years
  - Beta-blocker with ischemic heart disease
  - Antihypertensive if blood pressure consistently >160/90 or 140/90 if diabetic
  - ACE-I or ARB in diabetes with evidence or renal disease

- CNS
  - SSRI (or SNRI or pregabalin if SSRI contraindicated) for persistent severe anxiety that interferes with independent functioning
START Application

- Musculoskeletal System
- Vitamin D and calcium in patients with known osteoporosis, osteopenia, and/or previous fragility fracture
- Bone anti-resorptive or anabolic therapy in patients with documented osteoporosis, where no contraindication exists

START Application

- Vaccines
  - Trivalent influenza vaccine annually
  - Pneumococcal according to guidelines
STOPP/START Application
Unaddressed problems

- Drug-disease state interaction
  - Omeprazole-osteoporosis
- Appropriate duration of therapy
  - Alendronate
    - Drug holiday >5 years
- Prescribing omissions
  - Vaccines?

Determining Clinical Relevancy

Life Expectancy  Prioritization

Patient Assessment & Monitoring  Patient Preference & Clinical Experience

Medical Histories  Follow-up
### Application; patient assessment & Monitoring

#### Review of Systems

- **Psychiatric:** Depression controlled, *Occasional anxiety at bedtime*
- **Eyes:** No Blurred Vision, No Double Vision
- **Cardiovascular:** No Chest Discomfort, No Orthopnea, No Palpitations
- **Respiratory:** No Cough, No Dyspnea
- **Gastrointestinal:** *No Abdominal Pain or indigestion, No Constipation, No Diarrhea, No Dysphagia*
- **Neurological:** *Occasional dizziness, daytime somnolence, No Syncope, No Ataxia, No Paresthesias*
- **Musculoskeletal:** *Joint Pain, Myalgias, Muscle Weakness, Impaired Mobility*
- **Integumentary:** No Decubitus Ulcerations, No Rash
- **Endocrinology:** No Goiter, No Polyphagia, No Polydipsia

![Vitals Chart]

- **Estimated CrCl 20-25mL/min**
- **A1C 6.6**
- **Vitals:** BP 140/90mmHG, Pulse 82

### Application; Prioritize

- Long-acting benzodiazepine + anticholinergic
- Chronic NSAID use with impaired renal function & warfarin
- Calcium/vitamin D prescribing omission
- Prolonged bisphosphonate use with GERD
- Prolonged “high dose” PPI with osteoporosis
- HTN & diabetes prescribing omissions?
- Preventative therapy for ASCVD?
- “low dose” digoxin therapy
- Vaccines?
Patient Preference, Clinical Experience, & Follow-up

- Discuss risks and benefits of each medication
- Use patient-centered approach
- Discuss with caregivers
- Gradual dose reductions with psychotropics!
- Discontinuations when ADEs or lack of efficacy
- Provide updated medication list
- Counsel on medications
- Determine follow-up
- Monitor changes
- Implement further changes

QUESTIONS?
References