Starting and Stopping Medications in the Elderly

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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

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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

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Pharmacokinetics & Pharmacodynamics

Pharmacokinetics

- Effect of body on drug
- **ADME**
- **A**bsorption→ **D**istribution→ **M**etabolism→ **E**xcretion

Pharmacodynamics

- Effect of drug on body
- Medication exhibiting its pharmacologic effect

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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

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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

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Geriatric Distribution

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

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Geriatric Metabolism

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

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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

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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

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

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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

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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.

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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
- Improving Prescribing in the Elderly Tool, "The Canadian Criteria", 2000.

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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

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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

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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**

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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
- Originally published in 2008, updated 2014
- Criteria developed through expert consensus from literature review

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STOPP/START Categories

STOPP

- Indication
- Cardiovascular system
- Antiplatelet/anticoagulant drugs
- CNS & psychoactive drugs
- Renal System
- GI System
- Respiratory system
- Muscoskeletal 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

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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**

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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*

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!!!

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

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PIM Comparison

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

*use with caution

- 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

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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
- Polyethlene glycol 17G daily
- Omeprazole 40mg daily
- Alendronate 70mg daily x 5 years
- Sertraline 50mg PO daily
- Diphenhydramine 50mg PRN sleep
- Clonazepam 1mg PO q12h

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BEERS criteria application PIMs

Medication	Rationale	Recommendation	Quality	Strength
Digoxin	a.Fib &CHF : more effective alternatives, may be associated with increased mortality	Avoid	Moderate	Strong
Diphenhy-dramine	Highly anticholinergic, clearance reduced, tolerance when used as a hypnotic	Avoid	Moderate	Strong
Benzodiaze-pines	Increased sensitivity, decreased metabolism of long-acting agents, increased risk of cognitive impairment, delirum, falls fractures	Avoid	Moderate	Strong

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Beers Criteria Application PIMs

Medication	Rationale	Recommendation	Quality	Strength
Proton-pump inhibitors	Risk of c diff, bone loss, fractures	Avoid >8 weeks, unless high risk	High	Strong
NSAIDs	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	Avoid chronic use, unless other alternatives are not effective and patient can take gastroprotective agent	Moderate	Strong

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Beers Criteria Application Drug-Disease Interactions

Disease	Medication(s)	Rationale	Recomm-endation	Quality	Strength
History of falls or fractures	Anticonvulsants Antipsychotics Benzodiazepines Hypnotics TCAs SSRIs Opioids	Ataxia, impaired psychomotor function, syncope, falls. Shorter acting benzodiazepine preferred. If needed, consider reducing other CNS-active medications to	Avoid	Moderate	Strong
Dementia or cognitive impairment	Anticholinergics Benzodiapines H2-receptor antagonists Hypnotics Antipsychotics	Adverse CNS effects Antipsychotics associated with increased risk of CVA and mortality in patients with dementia	Avoid	Moderate	Strong

Beers Criteria Application
Drugs to Use with Caution

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

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Beers Criteria Application
Drug-drug Interactions

Drug or class	Interacting drug or class	Rationale	Recommendation	Quality	Strength
Antidepressants Antipsychotics Benzodiazepines Hypnotics	≥2 other CNS-active drugs	Increased risk of falls and fractures	Avoid ≥3 CNS-active drugs, minimize use	Moderate-High	Strong
Warfarin	NSAIDs	Increased risk of bleeding	Avoid when possible, monitor for bleeding	High	Strong

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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?

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STOPP Application

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

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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 eGDR < 30mL/min/1.73m (risk of digoxin toxicity)
  - NSAID's if eGFR <10mL/min/1.73m2

STOPP Application

- Gastrointestinal System
  - PPI for uncomplicated peptic ulcer disease for >8weeks (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)

STOPP Application

- 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

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START Application

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

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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?

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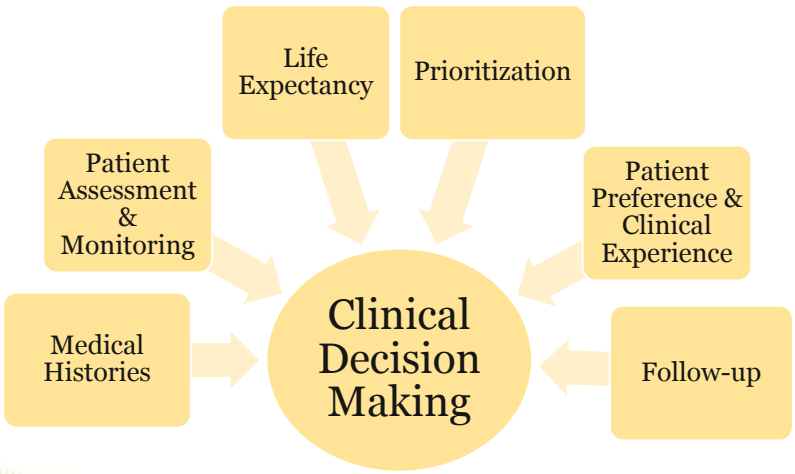
Determining Clinical Relevancy



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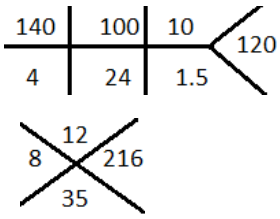
Application; patient assessment & Monitoring



Estimated CrCl 20-25mL/min

A1C 6.6

Vitals: BP 140/90mmHG
Pulse 82

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

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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?

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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

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QUESTIONS?

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