Inappropriate Medication Use in the Elderly

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Disclosures

• The presenters have no actual or potential conflict of interest in relation to this presentation
Objectives

At the end of this program, the learner will be able to:

1. Explain physiologic changes related to medication use that occur in older adults
2. Identify potentially inappropriate medications (PIM) for older adults
3. Understand risks of using specific PIM in older adults
4. Recommend non-pharmacological and pharmacological alternatives for older adults
Statistics

- Global population >65 years expected to be 22% in 2050 (up from 11% in 2010)
- 35% of ED visits for adverse drug events (ADEs)
- 7 times more likely to be hospitalized due to ADE
- 27% ADEs could be prevented in primary care
  - 42% in long-term care
- PIM = $7.2 billion in healthcare expenditures
Why So Many ADEs in Older Adults?

- Age-related physiologic changes
- Comorbidities
- Poly pharmacy
  - PIM
- Lack of trials
Potentially Inappropriate Medications

• Linked strongly with poor patient outcomes
  – ADEs, hospitalizations, death
• Some have limited effectiveness in older adults
• Some associated with serious problems
  – Delirium, falls, fractures, etc.
• Clinical judgment on individual basis
Age-Related Physiologic Changes
Age-Related Pharmacokinetic Changes

• Absorption
  – Reduced gastric acid secretion
    • Decreased bioavailability
      – Ex: calcium, iron
  – Reduced GI motility and blood flow
  – Reduced hepatic blood flow (↓ first past extraction)
    • Increased bioavailability
      – Ex: morphine
Age-Related Pharmacokinetic Changes

• Distribution
  – Less lean body mass
  – Less total body water
  – Increased body fat
• Hydrophilic medications
  » ↑ concentrations
• Lipophilic medications
  » ↑Vd, ↓ concentrations, delayed onset, ↑ t\(_{1/2}\)
Age-Related Pharmacokinetic Changes

• Metabolism
  – Reduced liver blood flow
    • Effects depend on each drug
    • ↓ Phase I metabolism = increased bioavailability
    • No change in Phase 2 metabolism
    • Prodrugs = reduced/slowed bioavailability

• Elimination
  – Kidney – reduced function
    • GFR ≈ creatinine clearance (CrCl)
    • Cockroft and Gault equation
Estimating Renal Function

- Cockroft and Gault equation

\[
CrCl = \frac{(140 - \text{age}) \times (\text{IBW})}{72 \times \text{Scr}} \times 0.85
\]

(if female)
Pharmacodynamics - Considerations

- What the drug does to the body

<table>
<thead>
<tr>
<th>DRUG</th>
<th>PD EFFECT</th>
<th>CAUSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam</td>
<td>↑ sedation</td>
<td>↓ Phase 1 hepatic metabolism</td>
</tr>
<tr>
<td>Morphine</td>
<td>↑ analgesia</td>
<td>↓ hepatic metabolism</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>↓ cognitive function</td>
<td>↓ cholinergic system function</td>
</tr>
<tr>
<td>Warfarin</td>
<td>↑ anticoagulation</td>
<td>↑ inhibition of factors II, VII, IX, X</td>
</tr>
</tbody>
</table>

Case Question

- CC is a 69 year old male
  - 6’ 3” 107 kg (IBW = 84.5)

Which physiologic change(s) have likely occurred?

a. Increased gastric acid secretion
b. Reduced body fat
c. Reduced liver blood flow
d. Reduced elimination (CrCl)
e. C & D
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Tools to Evaluate PIM Use
Various Tools to Prevent PIM

• Over 46 tools identified
  – 20 referred to previously published tools
  – 36 targeted geriatric population
  – 14 focused on over-prescribing
  – Most not clinically validated
Various Tools to Prevent PIM

• Beers Criteria
  – Significant correlation with negative clinical outcomes

• Less-studied tools
  – Kaiser Permanente Model
  – Lipton Criteria
  – STOPP Criteria
  – NCQA Criteria
Using Tools to Evaluate PIMs

• Intentions:
  – Improve medication selection
  – Educate clinicians and patients
  – Reduce ADRs

• Use common sense & clinical judgement
Key Considerations

- Potentially inappropriate meds, not definitely
- Evaluate patient-specific factors
- Understand rationale for inclusion of meds
  - Caveats exist for most meds
- Recommend safer non-pharmacological and pharmacological options
  - Includes lifestyle changes

= alternative
= new in 2015
Beers Criteria

• Goal: To improve the care of older adults by reducing their exposure to PIM
• Started in 1991
• Intended to:
  – Improve medication selection
  – Educate clinicians and patients
  – Reduce ADEs
  – Evaluate quality of care in older adults
Beers Criteria – 2015 Updates

PIMs and older adults

• Nitrofurantoin
• Antiarrhythmics
• Sedative-hypnotics
• PPI use over 8 weeks
• Desmopressin for nocturnal polyuria

Drug-disease PIMs

• Sedative-hypnotics in dementia/cognitive impairment
• Opioids in fall or fracture risk

<table>
<thead>
<tr>
<th>Avoid in most older adults</th>
<th>Avoid with specific diseases / symptoms</th>
<th>Use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>*excludes antimicrobials</td>
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<td></td>
</tr>
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Medications to Avoid in Most Older Adults

*High* Quality of Evidence

*Strong* Recommendation to Avoid
Certain Antiarrhythmics

• Removed recommendation to avoid class Ia, Ic, III antiarrhythmics

• Rate vs rhythm control:
  – Similar rates of mortality and morbidity
  – Rate control may be preferred in older adults
    • Reduced risk of toxicities
    • Lower cost
    • Simplification
Potentially Inappropriate Antiarrhythmics

- **Amiodarone**
  - Toxicities include thyroid disease, pulmonary disorders, QT-interval prolongation
  - Avoid as first-line A.fib, unless CHF or LVH

- **Dronedarone**
  - Poor outcomes in A.fib and heart failure

- **Digoxin**
  - Avoid doses > 0.125 mg for any indication
  - Avoid as first line in A.fib

- **Disopyramide**
  - Highly anticholinergic
  - May induce CHF
Antidepressants

• Tricyclic Antidepressants
  – Amitriptyline, clomipramine, doxepin (doses >6 g/d), imipramine, nortriptyline, desipramine
  – Highly anticholinergic
    • Dry mouth, constipation, urinary retention, confusion
  – Sedating
  – Orthostatic hypotension

• SSRIs
  – Paroxetine: Highly anticholinergic
  – Citalopram at doses >20mg/day

Sulfonylureas, Long-Duration

• Glyburide
  – Risk of prolonged hypoglycemia

• Chlorpropamide
  – Risk of prolonged hypoglycemia
  – Risk of SIADH (syndrome of inappropriate antidiuretic hormone secretion)

• Alternatives
  – Glimepiride, glipizide (avoid XL formulation)
Proton Pump Inhibitors

- Omeprazole, pantoprazole, lansoprazole, etc
- Associated with C. diff infection, bone loss, and cognitive impairment
- Avoid scheduled use for >8 weeks, unless:
  - High-risk patients (oral corticosteroid use, chronic NSAIDS)
  - Erosive or Barret’s esophagitis
  - Failure of alternative agents

Alternatives: H2RAs, as needed calcium carbonate, lifestyle modifications
Case Question

• RH is a 68 YOM who struggles with controlling his diabetes and often has issues with hypoglycemia.

• Which of RH’s diabetes medications has an increased risk of prolonged hypoglycemia?
  a) exanatide  
  b) glyburide  
  c) metformin  
  d) sitagliptin
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Medications to Avoid in Most Older Adults

*Moderate* Quality of Evidence
Strong Recommendation to Avoid
First-Generation Antihistamines

- Hydroxyzine
- Promethazine
- Meclizine
- Diphenhydramine (oral)
- Chlorpheniramine

- Nasal saline spray
- Loratadine, cetirizine
- Intranasal corticosteroid

- Highly anticholinergic
  - Confusion
  - Dry mouth
  - Constipation
  - Urinary retention

- Reduced clearance with older age
- Tolerance develops when used as hypnotic

*diphenhydramine - may be appropriate for acute severe allergic reactions in certain situations*
Benzodiazepines

- Increased sensitivity, slower metabolism
- Risk of delirium, falls, fractures, cognitive impairment
- **AVOID** for treatment of insomnia, agitation, delirium
- May be appropriate for some situations
- Preferred in the elderly:
  - Lorazepam, oxazepam, temazepam ➔ LOT

- Anxiety – *buspirone, SNRI*
- Sleep – *non-pharmacological strategies*
Meperidine

- Not recommended in any population for pain control
- Nor-meperidine (active metabolite) accumulates
- Risk of neurotoxicity (seizures, tremors)
- Safer alternatives
  - Tramadol
  - Morphine
  - Oxycodone/acetaminophen
Antispasmodics

- Dicyclomine, scopolamine, belladonna alkaloids
- Highly anticholinergic
- Questionable effectiveness

- Alternatives for chronic constipation: fiber, fluids, polyethylene glycol, psyllium
- Alternatives for diarrhea: loperamide
Nitrofurantoin

- Antibiotic for urinary tract infections
- AVOID if CrCl less than 30 mL/min
  - Evidence suggests it can be used in CrCl <60 mL/min
  - Not recommended for long-term suppression
- May cause pulmonary fibrosis, hepatic toxicity
- Consider alternative antibiotics if able

Alpha-1 Blockers

• Doxazosin, prazosin, terazosin
• High risk of orthostatic hypotension & urinary incontinence
• Alternative agents have better benefit:risk ratio
  ✓ – ACE inhibitors/ARBs
  ✓ – Beta blockers
  ✓ – Calcium channel blockers
  ✓ – Thiazide diuretic
1\textsuperscript{st} and 2\textsuperscript{nd} Generation Antipsychotics

- Increased risk of stroke and mortality if dementia
- Acceptable uses
  - Schizophrenia
  - Bipolar disorder
  - Short-tern antiemetic during chemotherapy
- DO NOT use for dementia-related behavioral problems \textit{unless} non-pharmacological options have failed and patient threatens to harm self or others
Non-Benzodiazepine Hypnotics

- Eszopiclone, zolpidem, zaleplon
- Side effect profile similar to benzos
- Only slight improvement in sleep latency & duration
- Increased ED visits and hospitalizations
- Motor vehicle crashes

Avoid use - no caveats

Alternatives for insomnia
- Non-pharmacologic interventions
  - Low-dose trazodone or doxepin, ramelteon

Pharmacist’s Letter. 2012.
Oral NSAIDs

- Ibuprofen, naproxen, aspirin >325mg/day, ketorolac
- Increased risk of gastric bleed and peptic ulcer in high-risk groups:
  - Age >75 years
  - Corticosteroid use
  - Antiplatelet or anticoagulant use
- Use of concomitant PPI reduces, but does not eliminate risk
NSAIDs (Continued)

• **Alternatives**
  - Pain: hydrocodone/acetaminophen, oxycodone/acetaminophen
  - Neuropathic pain: duloxetine, venlafaxine, pregabalin, gabapentin
  - Acute gout: NSAIDs other than ketorolac and indomethacin, colchicine, prednisone
  - If chronic NSAID use necessary, combine with a PPI OR choose celecoxib (unless heart failure OR GI/CV risk too great)
Case Question

• AD is an 87 YOM who presents to the ED with increased confusion. He has a history of seasonal allergies and has been taking diphenhydramine for his symptoms.

• Which medication would you suggest that AD try for his seasonal allergies instead of diphenhydramine?

a. chlorpheniramine
b. loratadine
c. cetirizine
d. A or B
e. B or C
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e. B or C
Case Question

• AD is an 87 YOM who presents to the ED with increased confusion and a fall with a small laceration to the head. Per his son, he has been more confused than normal over the past two days and fell and hit his head on the kitchen counter while trying to take his dishes to the sink. A urine sample is collected and it appears cloudy.

• Which medications could have precipitated AD’s UTI?

a) Diphenhydramine, amitriptyline, doxazosin
b) Lisinopril, amitriptyline, doxazosin
c) Losartan, diphenhydramine, acetaminophen
d) Lisinopril, acetaminophen, meloxicam
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PIM in Older Adults with Specific Diseases
Heart Failure

- NSAIDs and celecoxib
- Diltiazem and verapamil
  - Avoid in systolic heart failure only
- Pioglitazone, rosiglitazone
- Cilostazol
- Dronedarone
  - severe or recently decompensated CHF

May promote fluid retention and trigger an exacerbation
Parkinson Disease

- Antipsychotics
  - EXCEPT aripiprazole, quetiapine and clozapine
- Metoclopramide
- Prochlorperazine
- Promethazine

May worsen parkinsonian symptoms
History of Falls/Fractures

• Anticonvulsants
  – Avoid except for seizure or mood disorders

• Opioids
  – Excludes pain due to recent fractures or joint replacement

• Benzodiazepines & nonbenzodiazepine hypnotics

• TCAs & SSRIs

• May cause psychomotor impairment, ataxia, syncope, falls

• If must be used
  – Reduce dose of other CNS medications with fall risk
  – Encourage other fall reduction strategies
Chronic Constipation

- Antimuscarinics for urinary incontinence
  - Darifenacin, oxybutynin, solifenacin, tolterodine
  - Variable responses
- Calcium channel blockers
  - Diltiazem, verapamil
- 1st generation antihistamines
  - Diphenhydramine, hydroxyzine, promethazine
- Anticholinergics and antispasmodics

*May worsen constipation*

Case Question

- RH is a 68 YOM who was admitted to your hospital for shortness of breath and bilateral pitting edema in the lower extremities.

- Which medication likely precipitated RH’s recent CHF exacerbation?

  a) enalapril
  b) metoprolol
  c) sitagliptin
  d) naproxen
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Use with Caution
Medications to Use with Caution

• Medications that are appropriate in some patients
• Significant risk for misuse or harm
• No changes from 2012 updates
Drug-Drug Interactions
Drug-Drug Interactions

• Interactions highly associated with negative outcomes in older adults
• Not all-inclusive
• All strong recommendations

# Medications Interaction Recommendation

## Increased risk of falls

- Benzos/sedative hypnotics
- Opioids
- ≥ 2 other CNS-active drugs

- Avoid total of ≥ 3 CNS drugs
- Minimize # of CNS drugs

## Increased risk of bleeding

- Warfarin
- NSAIDs

- Avoid when possible
- If used, monitor closely
## Medications Interaction Recommendation

### Increased risk of falls & cognitive decline
- **Antipsychotics**  
- **Antidepressants**  
- **Anticholinergics**  

≥ 2 other CNS-active agents  

- Avoid total of ≥ 3 CNS drugs  
- Minimize # of CNS drugs  
- Minimize # of anticholinergics

### Increased risk of lithium toxicity
- **Lithium**  
  ACEIs  
  Loop diuretics  

- Avoid  
- Monitor lithium levels

### Increased risk of urinary incontinence
- **Peripheral alpha-1 blockers**  
  Loop diuretics  

- Avoid in women, unless conditions warrant both drugs

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PIMs Based on Renal Function
PIMs Based on Renal Function

- Adapted from previously published criteria

<table>
<thead>
<tr>
<th>CrCl cutoff</th>
<th>Medication</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30 mL/min</td>
<td>Amiloride Dabigatran Rivaroxaban Spironolactone Triamterene</td>
<td>Avoid</td>
</tr>
<tr>
<td>&lt; 30 mL/min</td>
<td>Colchicine</td>
<td>Reduce dose</td>
</tr>
<tr>
<td>&lt; 25 mL/min</td>
<td>Apixaban</td>
<td>Avoid</td>
</tr>
<tr>
<td>&lt; 50 mL/min</td>
<td>H₂ RAs</td>
<td>Reduce dose</td>
</tr>
<tr>
<td>&lt; 60 mL/min</td>
<td>Gabapentin Pregabalin</td>
<td>Reduce dose</td>
</tr>
<tr>
<td>≤ 80 mL/min</td>
<td>Levetiracetam</td>
<td>Reduce dose</td>
</tr>
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</table>
STOPP/START Criteria
STOPP/START Criteria

• “Screening Tool of Older Persons’ Prescriptions”
• “Screening Tool to Alert to the Right Treatment”
• European Geriatric Medicine
• Deficiencies in Beers Criteria
  – Some drugs are obsolete (in Europe) or less relevant
  – Several drugs not contraindicated in elderly
  – No mention of errors of omission in prescribing
  – Do not address drug class duplication issues
STOPP/START Criteria Goals

- Goals:
  - Discuss significant and common PIMs
  - Organized into physiological systems
  - Give special attention to PIMs in patients with fall risk, opiate use, drug class duplication
  - Address prescribing omissions
  - Assist in preventing hospital readmissions

- Criteria represents the views of a panel of geriatric experts

Differences from Beers List

- PIM examples not mentioned in Beers Criteria:
  - Furosemide for ankle edema (no signs of CHF)
  - Thiazide diuretics in patients with history of gout
  - NSAID with moderate to severe hypertension, CHF or chronic renal failure
  - Chronic opioids with constipation and no appropriate bowel regimen
STOPP Examples

- Lists medications in a certain situation
- STOPP examples:
  - Aspirin with history of peptic ulcer without H2 antagonist or PPI
  - SSRIs with history of clinically significant hyponatremia
  - Systemic corticosteroids instead of inhaled corticosteroids for COPD maintenance therapy
  - Corticosteroids for >3 months as monotherapy for RA or OA
  - Beta blockers in diabetic patients with frequent hypoglycemic episodes

STOPP/START Criteria

- Patients prone to falls
  - Benzodiazepines, neuroleptics, first generation antihistamines, long term opiates, vasodilators known to cause hypotension
- Duplicate drug classes
  - Single agent optimization before adding a second agent from the same class
    - example exclusion: pain management
START Examples

• 44-57% of elderly in the hospital lack one or more indicated medication

• START: consider in patients >65 with appropriate indications
  – Warfarin in patients with chronic atrial fibrillation
  – Statin therapy with documented history of vascular disease, independent functional status, life expectancy >5 years
  – Home continuous oxygen in chronic respiratory failure
  – Antidepressant with moderate to severe symptoms for >3 months
  – Antiplatelet and statin therapy in diabetes with comorbid conditions
Case Question

- MM is a 72 YOF who has a history of Parkinson’s, chronic lower back pain, heart failure and constipation.

- What may be an appropriate addition to MM’s home medication list?

  a) Morphine SR to better control her pain
  b) Naproxen to help pain and inflammation
  c) Docusate daily to help with constipation
  d) Senna-S daily to help with constipation
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Conclusions

• Many physiologic changes occur in older adults
  – May alter medication effects

• The Beers and STOPP/START criteria include many medications that are usually not recommended to be used in older adults, however they may be appropriate for some patients in some situations
  – Must look at patient-specific factors and use clinical judgement
References

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