Applying Clinical Pharmacology Principles to Improve Care for the Older Adult

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Learning Objectives

• Describe the role of PK/PD in defining potentially inappropriate medications for older adults
• Consider multimorbidity, aging, frailty, polypharmacy and drug interactions in therapeutic decision making for older adults
• Identify opportunities for improving pharmacotherapy outcomes for older adults, including deprescribing
Health Outcomes
- Length of Life (50%)
- Quality of Life (50%)

Health Factors
- Health Behaviors (30%)
  - Tobacco Use
  - Diet & Exercise
  - Alcohol & Drug Use
  - Sexual Activity
- Clinical Care (20%)
  - Access to Care
  - Quality of Care
- Social & Economic Factors (40%)
  - Education
  - Employment
  - Income
  - Family & Social Support
  - Community Safety
- Physical Environment (10%)
  - Air & Water Quality
  - Housing & Transit

Policies & Programs

http://www.countyhealthrankings.org(county-health-rankings-model)
Figure 4. Percent distribution of number of diagnosed chronic conditions at office-based physician visits for adults with hypertension, by age: United States, 2013

Note: Estimates may not add to 100 due to rounding.

1Percentage for those aged 45–64, 65–74, and 75 and over is significantly different from those aged 18–44 (p < 0.05).

2Percentage for those aged 65–74 and 75 and over is significantly different from those aged 45–64 (p < 0.05).


https://www.cdc.gov/nchs/products/databriefs/db263.htm
Pharmacokinetics, Pharmacodynamics and Aging

**PK**
- Concentration in the Circulation
  - Absorption
  - Distribution
  - Metabolism
  - Excretion

**PD**
- Drug Effect
  - Drug-receptor interactions
  - Concentration at receptor
  - Homeostatic mechanisms

**Efficacy**
- Desirable Therapeutic Outcome
  - disease characteristics
  - other medications
  - Adherence
  - Health behaviors and social determinants of health
Medications: The Right Balance

“Medications are probably the single most important health care technology in preventing illness and disability in the older population.”

"Any symptom in an elderly patient should be considered a drug side effect until proven otherwise."

A Case Study

• Ms. S is a 78 year-old living independently in a senior affordable housing apartment building.

• Her current diagnoses (self-report) include:
  • Chronic pain (knee and hip)
  • Schizophrenia
  • Hypertension
  • Anxiety
  • Depression
  • GERD
  • Incontinence

• She has a behavioral health case manager and currently sees a pain specialist, a psychiatrist and a primary care provider. She frequently changes providers and visits the ER multiple times per year.
A Case Study

- She is experiencing difficulty with doing her laundry and preparing meals, and is using a wheelchair to navigate outside of her apartment.
- She is wearing incontinence underwear every day, but is having trouble affording them.
- She is a smoker.
- She has a long history of opioid use for chronic pain. Providers have stopped prescribing them to her in the past, but she changes providers or goes to the ER for new prescriptions. She admits to selling the opioids to purchase food and prescriptions at times and also reports occasional use at higher than the prescribed dose.
- She has a fall and ER visit the evening before her clinic visit.
A Case Study

Trazodone 50 mg QHS
Lurasidone 80 mg QHS
Perphenazine 4 mg BID
Bupropion 100 mg BID
Hydroxyzine 50 mg TID
Losartan 100 mg QD
Atorvastatin 40 mg QHS
Aspirin 81 mg QD
Clonidine 0.2 mg TID
Hydralazine 50 mg TID
Omeprazole 40 mg QD

Diclofenac gel as needed
Gabapentin 800 mg TID
Acetaminophen/Diphenhydramine QHS
Ibuprofen 800 mg BID—taking as many as 5 per day
Acetaminophen/Oxycodone 325 mg/7.5 mg: 1 tablet TID
Linaclotide 290 mcg QD
Senna OTC 4 tabs as needed
Kidney Function and Older Adults: Gabapentin

Age: The effect of age was studied in subjects 20-80 years of age. Apparent oral clearance (CL/F) of gabapentin decreased as age increased, from about 225 mL/min in those under 30 years of age to about 125 mL/min in those over 70 years of age. Renal clearance (CLR) and CLR adjusted for body surface area also declined with age; however, the decline in the renal clearance of gabapentin with age can largely be explained by the decline in renal function. Reduction of gabapentin dose may be required in patients who have age related compromised renal function. (See PRECAUTIONS, Geriatric Use, and DOSAGE AND ADMINISTRATION.)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020235s041,020882s028,021129s027lbl.pdf

<table>
<thead>
<tr>
<th>Medication Class and Medication</th>
<th>Creatinine Clearance, mL/min, at Which Action Required</th>
<th>Recommendation, Rationale, QE, SR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system and analgesics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duloxetine</td>
<td>&lt;30</td>
<td>Avoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased gastrointestinal adverse effects (nausea, diarrhea)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>QE = Moderate; SR = Weak</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>&lt;60</td>
<td>Reduce dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNS adverse effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>QE = Moderate; SR = Strong</td>
</tr>
</tbody>
</table>

Pharmacodynamic Differences with Aging

Figure. (A) Baseline and (B) sensitivity differences between young and elderly adults. $E_0$ = baseline effect before drug administration when drug concentrations are zero.

A POCKET GUIDE TO THE
2019 AGS BEERS CRITERIA®

This guide has been developed as a tool to assist healthcare providers in improving medication safety in older adults. The role of this guide is to inform clinical decision-making, research, training, quality measures and regulations concerning the prescribing of medications for older adults to improve safety and quality of care. It is based on the 2019 AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults.

Originally conceived of in 1991 by the late Mark Beers, MD, a geriatrician, the Beers Criteria catalogues medications that cause side effects in the elderly due to the physiologic changes of aging. In 2011, the AGS sponsored its first update of the criteria, assembling a team of experts and using an enhanced, evidence-based methodology. Since 2011, the AGS has been the steward of the criteria and has produced updates using an evidence-based methodology and rating each Criterion (quality of evidence and strength of evidence) using the American College of Physicians’ Guideline Grading System, which is based on the GRADE scheme developed by Guyatt et al.

The full document, along with accompanying resources can be found in their entirety online at geriatricscareonline.org.

INTENDED USE
The goal of this guide is to improve care of older adults by reducing their exposure to Potentially Inappropriate Medications (PIMS).

- This should be viewed as a guideline for identifying medications for which the risks of their use in older adults outweigh the benefits.
- These criteria are not meant to be applied in a punitive manner.
- This list is not meant to supersede clinical judgment or an individual patient’s values and needs. Prescribing and managing disease conditions should be individualized and involve shared decision-making.
- These criteria also underscore the importance of using a team approach to prescribing and the use of non-pharmacological approaches and of having economic and organizational incentives for this type of model.

A companion piece that addresses the best way for patients, providers, and health systems to use (and not use) the AGS Beers Criteria® was also developed. The

Prescribing Decisions in Patients with Reduced Life Expectancy

Guiding Principles for the Care of Older Adults with Multimorbidity

<table>
<thead>
<tr>
<th>Guiding Principle II: Interpreting the Evidence Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recognizing the limitations of the evidence base, interpret and apply the medical literature specifically to older adults with multimorbidity.</td>
</tr>
</tbody>
</table>

How to Use in Clinical Practice

<table>
<thead>
<tr>
<th>Goal</th>
<th>Implementation Strategies &amp; Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider certain key principles in evaluating clinical evidence.</td>
<td>Consider:</td>
</tr>
<tr>
<td></td>
<td>• Applicability and quality of evidence;</td>
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<tr>
<td></td>
<td>• Outcomes;</td>
</tr>
<tr>
<td></td>
<td>• Harms and burdens;</td>
</tr>
<tr>
<td></td>
<td>• Absolute risk reduction;</td>
</tr>
<tr>
<td></td>
<td>• Time horizon to benefit.</td>
</tr>
</tbody>
</table>
Guiding Principles for the Care of Older Adults with Multimorbidity

### Guiding Principle V: Optimizing Therapies and Care Plans Domain

Frame clinical management decisions within the context of risks, burdens, benefits, and prognosis (e.g., remaining life expectancy, functional status, quality of life) for older adults with multimorbidity.

#### How to Use in Clinical Practice

<table>
<thead>
<tr>
<th>Goal</th>
<th>Tools, Resources, Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify interventions that should not be initiated or should be stopped. Identify interventions that should be started.</td>
<td>• Factors to consider include:</td>
</tr>
<tr>
<td></td>
<td>1. Likelihood of benefit in terms of altering the person’s baseline risk for the particular outcome;</td>
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<tr>
<td></td>
<td>2. Risk of harm;</td>
</tr>
<tr>
<td></td>
<td>3. Difference between the time horizon to benefit and the patient’s likely remaining life expectancy (prognosis).</td>
</tr>
</tbody>
</table>

What Do We Need to Support Better Prescribing? A Call to Action

- Biomarkers of “physiological age”
- Evidence for likelihood of benefit and/or harm
- Evidence for time until benefit and/or time until harm
- Evidence for understanding treatment interactions
- Evidence to optimize dosing in multimorbidity
- Evidence to support optimal deprescribing
  - Deprescribing.org