Polypharmacy: What the Nurse Practitioner Should Know
Audrey M. Stevenson PhD, MPH, MSN, FNP-BC
Las Vegas 2017

Disclosure
I have no current affiliation or financial arrangement with any grantor or commercial interests that might have direct interest in the subject matter of this CE program.

Audrey M. Stevenson
August 2017

Objectives
- Name 5 physiological changes of aging that could impact pharmacokinetics and pharmacodynamics in older adults
- Compare and contrast the Beer’s criteria with other criteria sets
- State several adverse effects associated with anticholinergic drugs and list those drugs with the highest anticholinergic activity
- Identify the components of a stepwise approach to prescribing
What is Polypharmacy

- The use of multiple medications simultaneously
  - Rx
  - OTC
  - Herbal

Population

- ~43.1 million individuals over the age of 65
- Older adults over the age of 65 are treated with increasing numbers of drugs
- Multimorbidity in the elderly population ranges from 40% - 80%

Background

- Prescription Use in Older Adults
  - 1 Rx = 87%
  - ≥5 Rx = 36% (65-85 years)
  - 38% use at least 1 OTC
  - 75% of ambulatory adults over 75 years use at least 1 prescription and 1 supplement
  - 75% of adults over 18 do not report unconventional therapies to their clinician
Herbal and Dietary Supplements

- 14% in 1998 to 63% in 2010
- 75% of adults over the age of 75 years used at least one prescription drug and one dietary supplement

Pathophysiological Principles of Aging

Physiologic Changes of Aging

- Eye: Lens becomes rigid
- Hearing: High level hearing loss
- Body fat: 14% in young person – 30% in person aged 70
- Body water: 61% – 53%
- Liver: Decreased hepatic mass ad enzyme production, histologic changes
- Kidney: Decreased GFR (10 % per year after age 40) reduced ability to concentrate urine and sodium loss
Physiologic Changes of Aging

- Brain: Atrophic and circulatory changes

Pharmacokinetics and Pharmacodynamics

Changes from Aging

- The metabolism and excretion of many drugs decrease, requiring that doses of some drugs be adjusted.
- Toxicity may develop slowly because levels of chronically used drugs increase for 5 to 6 half-lives, until a steady state is achieved.
Pharmacokinetics (how the body handles and disposes of drugs via:
- Absorption
- Distribution
- Receptor sensitivity
- Metabolism
- Elimination

Pharmacokinetics and Pharmacodynamics

Absorption
- GI tract
  - Slowed GI motility
  - Decreased gastric acid production
  - Diminished transport mechanisms

Absorption
- Despite an age-related decrease in small-bowel surface area, slowed gastric emptying, and an increase in gastric pH, changes in drug absorption tend to be clinically inconsequential for most drugs.
  - Increases in gastric pH
  - Enteric coated tablets
First pass through the liver
- Less efficient

Plasma Protein Albumin
- Decreased binding sites for meds

Overall hepatic metabolism of many drugs through the cytochrome P-450 enzyme system decreases with age.
- For drugs with decreased hepatic metabolism, clearance typically decreases 30 to 40%.

Increased body fat
- Lipid soluble medications
With age, body fat generally increases and total body water decreases. Increased fat increases the volume of distribution for highly lipophilic drugs (e.g., diazepam, chlordiazepoxide) and may increase their elimination half-lives.

Distribution

- Decreased renal function
  - Elimination of drugs a longer process

Excretion

- After age 30, creatinine clearance decreases an average of 8 mL/min/1.73 m²/decade; however, the age-related decrease varies substantially from person to person.
- Serum creatinine levels often remain within normal limits despite a decrease in GFR because the elderly generally have less muscle mass and are generally less physically active than younger adults and thus produce less creatinine.
- Maintenance of normal serum creatinine levels can mislead clinicians who assume those levels reflect normal kidney function. Decreases in tubular function with age parallel those in glomerular function.

Renal Elimination
Pharmacodynamics

- Processes by which drugs influence cell physiology
  - Body’s response and sensitivity to drugs at the effector organs.
  - Receptor sites
  - Neuronal and Vascular changes

Patient Characteristics and Lifestyle Factors

- Alcohol
  - Increase clearance of many meds -> less available for desired effect
- Smoking
  - May stimulate hepatic mechanisms to clear meds more quickly
- Nutrition
  - Certain substances can affect drug utilization

Herbal and Dietary Supplements

- Patients don’t routinely volunteer this information
- Concerns about herbal-drug interactions
- Source of information
Polypharmacy

- Use of multiple medications by a patient
  - Ranges from 5-10
  - May have different definitions
- Also includes OTC and herbal supplements
- More of a problem for older adults
  - More chronic conditions
  - The use of greater numbers of drug therapies increases the risk of an adverse drug event
- Prevalence of polypharmacy depends on the care setting.

Evaluating Polypharmacy

- Common problem of the elderly
- Encountered in all care settings

Top 5 Issues of Older Adults

- Arthritic Pain
- Heart Disease (#1 cause of death after age 65)
- Cancer (2nd cause of death after age 65)
- Asthma, COPD
- Alzheimer’s

Vann, MR, 2017
Other Issues affecting seniors
- Falls
- Substance Abuse
- Obesity
- Depression
- Poverty
- Shingles

Evaluating Polypharmacy
- Common problem of the elderly
- Encountered in all care settings

Adverse Drug Events
Impact on Older Adults of Polypharmacy

> Greater risk for adverse drug events due to metabolic changes and decreased drug clearance associated with aging (risk compounded by increasing number of drugs used)
> Increases the potential for drug-drug interactions and prescription of potentially inappropriate medications
> Is an independent risk factor for hip fractures in one study. Number of drugs may increase likelihood of falls.
> Prescribing cascades
> Medication adherence compounded by visual or cognitive compromise

Hypothetical patient

> COPD
> Type 2 diabetes
> Osteoporosis
> Hypertension
> Osteoarthritis

Risks for Polypharmacy

> Chronic conditions
> Multiple providers
> SES
> Generic vs. Brand name
> Hospitalization
> Infrequent healthcare visits
The “Beers List”

Beers Criteria

› **Beers criteria** — The Beers criteria, initially developed by an expert consensus panel in 1991 to target nursing home residents, are the most widely-cited criteria used to assess inappropriate drug prescribing.

› The panel produced a list of medications considered inappropriate for older patients, either because of ineffectiveness or high risk for adverse events.
Separate guidance on avoiding 13 combinations of medications known to cause harmful drug-drug interactions. (falls, fractures, or urinary incontinence)

A list of 20 potentially problematic medications to avoid or for which doses should be adjusted depending on an older person's kidney function. (could raise risks for nausea, diarrhea, bleeding, affect the brain and nervous system, changes in mental well-being, bone marrow toxicity)

Three new medications and two new classes of medications added to the Criteria.

2015 Beers Updates
Anticholinergics
Reduced clearance
- First generation anti histamines
Antiparkinsonian agents
Not recommended for extrapyramidal symptoms
- Bentropine (oral) Trihexphenidyl
Antithrombotics
Orthostatic hypotension
- Dipyridamole, oral short-acting
Nitrofurantoin
Avoid in those creatinine clear < 30ml/min

Drugs to Avoid
- Amitriptyline
- Atropine
- Clozapine
- Dicyclomine
- Doxepin
- L-hyoscyamine,
- Thioridazine
- Tolterodine

Drugs most highly associated with anticholinergic activity
Also associated
- Chlorpromazine
- Diphenhydramine
- Nortriptyline
- Olanzapine
- Oxybutynin
- Paroxetine

Drugs to avoid
- CV
  - Peripheral alpha-1 blockers
- Digoxin
- Barbiturates
- Benzodiazepines
- Growth Hormone
- Proton pump inhibitors
  - Avoid use as antihypertensive
  - Avoid as first-line therapy for A-fib
  - Drug dependence
  - Increased sensitivity
  - Numerous SE
  - Risk of c-diff
Anticholinergic Activity

- Adverse effects associated with anticholinergic use in older adults:
  - Memory impairment
  - Confusion
  - Hallucinations
  - Dry mouth
  - Blurred vision
  - Constipation
  - Nausea
  - Urinary retention
  - Impaired sweating
  - Tachycardia

Extent of the problem

- Study: Those taking anticholinergic drugs were at increased risk for cognitive decline and dementia risk decreased with medication discontinuation
- Study: Individuals followed over 10 years without baseline dementia had increased risk of dementia and Alzheimer's disease in a dose relationship with use of anticholinergic drug classes (first generation antihistamines, tricyclic antidepressants, and bladder antimucarnics)
- Study: use of anticholinergic medications associated with greater decline in cognition and increased mortality over a two year period

Drugs most highly associated with anticholinergic activity

- Amitriptyline
- Atropine
- Clozapine
- Dicyclomine
- Doxepin
- L-hyoscyamine
- Thioridazine
- Tolterodine
Also associated

- Chlorpromazine
- Diphenhydramine
- Nortriptyline
- Olanzapine
- Oxybutynin
- Paroxetine

10 Medications for Older Adults to Avoid

1. Avoid long-term use of NASIDs
2. Use Digoxin with caution
3. Avoid certain Diabetes Drugs (Glyburide and chlorpropamide)
4. Avoid muscle relaxants
5. Avoid certain Medications used for Anxiety or Insomnia (Benzodiazepines, zaleplon, zolpidem, eszopiclone)
6. Avoid certain Anticholinergic drugs (amitriptyline, imipramine, trihexphenidyl, dicyclomine)
7. Avoid meperidine
8. Avoid certain OTC (diphenhydramine, chlopheniramine)
9. If not being treated for psychosis AVOID using Antipsychotics
10. Avoid estrogen pills and patches

Stop and Start

HealthinAging.org
Other Criteria Sets

- **Screening Tool of Older Person’s Prescriptions (STOPP):**
  - Introduced in 2008
  - STOPP and Beers criteria overlapped in several areas, but earlier versions of the Beers criteria used in this comparison contained some drugs no longer in common use, and STOPP includes consideration of drug-drug interactions and duplication of drugs within a class. In two studies, STOPP identified a significantly higher proportion of older people requiring hospitalization as a result of a medication-related adverse event than did the 2003 Beers criteria.

- **The FORTA (Fit FOR the Aged):**
  - List identifies medications rated in four categories (clear benefit; proven but limited efficacy or some safety concerns; questionable efficacy or safety profile – consider alternative; clearly avoid and find alternative) with ratings based on the individual patient's indication for the medication.

Other Criteria Sets

- **The Centers for Medicare and Medicaid Services drug utilization review criteria target eight prescription drug classes (digoxin, calcium channel blockers, angiotensin-converting enzyme inhibitors, H-2 receptor antagonists, NSAIDs, benzodiazepines, antipsychotics, and antidepressants)**
- and focus on four types of prescribing problems (inappropriate dosage, inappropriate duration of therapy, duplication of therapies, and potential for drug-drug interactions).

Healthcare Financing

- **Practical suggestions on how to improve prescribing practices:**
  - Document the indication for a new drug therapy
  - Educate patients on the benefits and risks associated with the use of a new therapy
  - Maintain a current medication list
  - Document response to therapy
  - Periodically review the ongoing need for a drug therapy
Underutilization of Appropriate Medications

- Medication effectiveness
- Affordability
- Dose Availability

Adverse Drug Events

- Adverse Drug Events (ADES)
- Common in older adults
- Estimated in 35% of ambulatory adults
  - 29% of these reactions require hospitalization or provider care
  - May be identified incorrectly (falls, dementia, urinary incontinence)
Geriatric syndromes frequently impacted by ADEs

- Falls and orthostatic hypotension
  - Antihypertensives
  - Benzodiazepines
  - SSRIs

Cognitive disorders: delirium and dementia

- Benzodiazepines
- Anticholinergics
- Opiates
- Prednisone

Urinary frequency and incontinence

- Acetylcholinesterase inhibitors
- Diuretics
Anorexia
- Iron
- Metformin
- Acetylcholinesterase inhibitors
- SSRIs

Considerations in prescribing

Quality Measures of Prescribing
- Avoidance of inappropriate medications
- Appropriate use of indicated medications
- Monitoring for side effects and drug levels
- Avoidance of drug-drug interactions
- Involvement of the patient
- Integration of patient values
Assess the individual for total number of medications and for certain groups of medications that have potential for adverse outcomes:
- Beta blockers
- Antidepressants
- Antipsychotics
- Other psychotropics
- Pain medications
- Other medications listed in the Beers Criteria
- Vitamins and supplements
Review

- Review for possible:
  - Drug-drug interactions
  - Drug-disease interactions
  - Drug-body interactions (pharmacodynamics)
  - Impact on functional status (Timed Get Up and Go test)
  - Subclinical ADRs
  - Weigh individual medication benefits against primary body functions (appetite, weight, pain, mood, vision, hearing, bladder, bowel, skin, swallowing, activity level)

Minimize

- Minimize nonessential medications:
  - Eliminate those medications that lack evidence
  - Eliminate medications whose risks outweigh benefits and have high potential for negative impact on primary functions

Optimize

- Optimize by addressing:
  - Duplication
  - Redundancy
  - Adjust renally cleared medications to creatinine clearance (GFR)
  - Adjust oral hypoglycemic to blood sugar target and HbA1c
  - Consider gradual dose reduction (GDR) for antidepressants
  - Adjust beta blocker dose for pacemakers
  - Adjust anticoagulants by international normalized ratio (INR) guidelines and possible DDIs.
  - Adjust seizure medications with free phenytoin level
Reassess heart rate, blood pressure (postural), oxygen sat (>92%) at rest and activity. Also reassess:
- Functional status (Timed Get up and Go, ADLs)
- Cognitive status
- Clinical status
- Medication compliance

A Stepwise Approach to Prescribing
- TTB
- Review current drug therapy
- Discontinue unnecessary therapy
- Consider adverse drugs for any new symptom
- Consider nonpharmacologic approaches
- Substitute with safer alternatives
- Reduce the dose
- Simplify the dosing schedule
- Prescribe beneficial therapy

Time to Benefit
- TTB is defined as the time to significant benefit.
Review current drug therapy
- Is the indication still relevant?
- Other prescriber?
- Duplicate?
- Safer therapy?
- Changing meds?
- New therapy?

Discontinue unnecessary therapy
- What are the goals of care?
- Is the treatment preventative or therapeutic?

Case Study
Consider adverse drug events for any new symptom

- Prescribing Cascade-
  - Develops when an adverse drug event is misinterpreted as a new medical condition and additional drug therapy is initiated to treat this medical condition.
Consider nonpharmacologic approaches

- Lifestyle modification in lieu of meds
- Conservative management

Substitute with safer alternatives

- What is the patient’s underlying chronic conditions that place them at risk?
  - Renal impairment
  - GI bleeds
  - Heart failure
Reduce the Dose
- AE may be dose-related
- Use minimal dose required to obtain clinical benefit

Simplify the Dosing Schedule
- Consider the patient’s health literacy
- Cognitive state
- Mobility

Prescribe Beneficial Therapy
- The fewer-the-better may not be the best response
- Avoiding meds with known benefit
Approach to prescribing

- Regardless of the sequence of steps, what is essential in prescribing is to continually:
  - reappraise the patient’s medication regimen in light of his or her current clinical status,
  - the goals of care,
  - and the potential risk/benefits of each medication.

Summary

- Physiological changes of aging that can impact pharmacokinetics and pharmacodynamics in older adults
- Polypharmacy can have a number of adverse impacts on older adults
- There are a variety of medication errors that can occur when prescribing for older adults but NPs can eliminate many of the risk
- There are several resources available to help in determining the best prescribing for adults.

Conclusion
Prescribing for the older adult with multimorbidity

- Patient preference
- Interpreting the Evidence
- Prognosis
- Clinical Feasibility
- Risk vs. Benefit

Golden Rule of Prescribing for Older Adults

- Start low, go slow
- Make one change at a time
- Avoid prescribing cascade
- Facilitating adherence—pill organizer, minimize total doses. One drug, one problem, once daily
- Assess appropriateness/medication review

Case Study

- 79-year-old male resident of a LTC
  - History:
    - Type 2 diabetes, CAD, CAGS 2014, HTN, depression, CVA with residual, mild hemiplegia, osteoarthritis of knees and hips.
    - Has a newly dx stage 2 left heel ulcer*. (non-healing)
    - ADL: requires assistance to transfer from W/C to bed.
Results
› X-ray of L heel = no osteomyelitis
› HbA1c was 5.9
› Arterial dopplers = minimal PVD
› Pre-albumin and albumin levels wnl
› No anorexia observed
› Patient encouraged to move extremities on a scheduled basis
› CBC w/diff and basic metabolic panel = wnl
› Serum creatinine = 1.2 mg/dL

Medications
› Sotolol 80 mg BID
› ASA 325 mg/day
› Fentanyl patch 25 mg q 72 h
› Famotidine 20 mg gd
› Nitroglycerin S/L, prn
› Acetaminophen/hydrocodone 5/500 mg TID
› Sertraline 75 mg gd
› Simvastatin 20 mg gd
› Trazodone 25 mg gd
› Ibuprofen 800 mg po TID, prn

Vital Signs
› Pulse = 72/min
› BP = 120/70
› Afebrile
› Weight 132
Physical Exam

- Exam essential normal, except for residual weakness from his CVA.
- 2-cm x 1-cm stage 2 ulcer on L heel noted without purulence
- Pedal pulses diminished but palpable bilaterally
- No edema palpated on lower extremities

Anything you would recommend at this point?

Treatment

- Wound treatment continued
- Sotalol being held with continued monitoring of cardiac rhythm and blood pressure
Ulcer responded to this measure and healed completely in the next 2 weeks.

Outcome

› Nine medications
   – Beta blocker noted as suggested by step 1
   – Antidepressants sertraline and trazadone were noted for duplication
   – Beers Criteria list medications noted ibupronfen

ARMOR

Stepwise

› Assess:

  – Nine medications
    – Beta blocker noted as suggested by step 1
    – Antidepressants sertraline and trazadone were noted for duplication
    – Beers Criteria list medications noted ibupronfen
Drug to drug interaction with peripheral microcirculation
- Beta blocker (sotalol) was considered
- DDI between NTG and sotalol? (Hypotension is enhanced in older adults due to decreased baroreceptors response and decreased venous tone and hypotension).
- Potential of beta blocker for delayed healing in skin ulcer
- NSAID: cognitive impact and risk of falls

NSAID d/c
Trazadone d/c
Minimize

Medications adjusted for estimated creatinine clearance
Sotalol initially held for 2 weeks of observations
Optimize
Reassess

› Ulcer healed in 2 weeks
› Sotalol restarted at a dose adjusted for creatinine clearance

Case 2

› 77 year old female reports for Coumadin follow up. She was discharged from the hospital at 9:00 PM the previous night after being admitted for an episode of Afib. She shows you two different pill boxes that she has in her purse and states that she is confused about which medications to take.

Case 2 cont.

› She appears exhausted and states that she is confused about which medication that she should be taking. When you examine her discharge orders you note that she was to discontinue diltiazem due to severe constipation and begin Metoprolol upon hospital discharge.
You inspect her two pill boxes and notice that the Toprol XL and Diltiazem are both in her pill minders and she can't explain how she determines which pill minder she takes medications from.

Case 2

What factors contributed to her polypharmacy?

The Prescribing Cascade

77 yo woman with urgency, gets nifedipine for HTN
- Edema, constipation, impaired bladder emptying
- Nocturia, urgency, some UI
- OAB!
- Add antimuscarinic
- Constipation → Add laxative...
References


References


Questions?