

## Deprescribing in Older Adults

Melanie A. Dodd, Pharm.D., Ph.C., BCPS, FASHP  
Associate Dean for Clinical and Professor in Geriatrics  
The University of New Mexico College of Pharmacy

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## Disclosures

- Sunovion Pharmaceuticals
- Investigator initiated research

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## Learning Objectives

Following this presentation, the participants will be able to:

1. Describe the effects of aging on pharmacokinetic and pharmacodynamic parameters
2. Discuss principles of prescribing and deprescribing to avoid adverse drug effects
3. Identify and discuss management techniques for potentially inappropriate medications in a given older adult based on 2023 Beers' Criteria.

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## Case: AB 81 year-old female with Medicare insurance

### Problem List

- |                            |                          |
|----------------------------|--------------------------|
| 1. CVA X 6                 | 11. Urinary incontinence |
| 2. Osteoarthritis          | 12. Atrophic vaginitis   |
| 3. Chronic diarrhea        | 13. COPD                 |
| 4. Diabetes, type 2        | 14. Frequent falls       |
| 5. Peripheral neuropathy   |                          |
| 6. Coronary artery disease |                          |
| 7. Hypertension            |                          |
| 8. Hypothyroidism          |                          |
| 9. Hypercholesterolemia    |                          |
| 10. Osteopenia             |                          |

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## AB's Medications

- |   |   |
|---|---|
| 1. levothyroxine 75 mcg daily                       | 11. glipizide immediate release 10 mg twice daily   |
| 2. lovastatin 10 mg, 2 tablets at bedtime           | 12. conjugated estrogen vaginal cream twice weekly  |
| 3. clopidogrel 75 mg daily                          | 13. gabapentin 300 mg tid   |
| 4. nitroglycerin SL tabs 0.4mg prn                  | 14. amitriptyline 10 mg qhs   |
| 5. amlodipine 10 mg daily                           | 15. hydrocodone/ acetaminophen 5/325 mg, 1 tab every 4-6 hours prn pain (uses 3-4 tabs/day) |
| 6. furosemide 20 mg daily                           | 16. tolterodine 4 mg qhs  |
| 7. potassium 10 mEq, 2 tablets twice daily          | 17. albuterol MDI with chamber once weekly  |
| 8. clonidine 0.2 mg, 2 tablets twice daily          |   |
| 9. metoprolol 50 mg twice daily                     |   |
| 10. Novolin 70/30 vials, 25 units qam, 15 units qpm |   |

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## AB's Medications (continued)

19. docusate 100 mg bid
20. mineral oil prn constipation
21. glycerin suppositories prn constipation (uses about 2x/week)
22. aspirin 81 mg daily
23. diphenhydramine 25 mg at bedtime for sleep (uses 3-4 x/week)
24. glucosamine 2 caps qday
25. metformin 1000 mg bid

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## Case AB Objective:

### Vital Signs:

- BP 168/63 HR 79
- RR 24 Temp. 97.8°F
- Weight 177.9 lbs.
- Pain 1/10

### Lab Values:

- Na 140
- K 4.8
- Cl 104
- BUN 25
- Scr 1.3

- HbA1c 6.8%
- Mean blood glucose 164.8
- TSH 5.680
- Lipids
  - TC 144
  - TG 258
  - HDL 39
  - LDL 53
- PE: Bilateral LE edema

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## Why is medication management important in older adults?

- Persons aged 65 and older are prescribed the highest proportion of medications in relation to their percentage of the U.S. population
  - Now, 16.9% (NM=18.5%) of total population buy >34% of all prescription medications and >30% OTC medications
  - Estimated by 2040, 25% of total population will buy 50% of all prescription drugs

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## Adverse drug events in older adults

- ADEs are responsible for 5% to 28% of acute geriatric hospital admissions
- ADEs occur in 35% of community-dwelling elderly persons
- ADEs incidence: 26/1000 hospital beds
- In nursing homes, \$1.33 spent on ADEs for every \$1.00 spent on medications

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## Risk of adverse drug events in older adults

- Increased risk of adverse drug events
  - Multiple medications
    - >50% of elderly use 4 or more medications
    - Increased frequency of drug-drug interactions
    - Decreased medication adherence
  - Multiple comorbidities
  - Age-related changes in drug pharmacokinetics
  - Age-related changes in drug pharmacodynamics

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## PHARMACOKINETICS



- Absorption
- Distribution
- Metabolism
- Elimination

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## Pharmacodynamics

- Definition
  - Time course and intensity of pharmacologic effect of a drug
  - Impairment varies considerably from person to person
  - All organ systems are affected
  - Kidneys, liver, GI, CNS, CV, GU

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### Altered Pharmacodynamic Mechanisms

- Change in receptor numbers
- Change in receptor affinity
- Postreceptor alterations
- Age-related impairment of homeostatic mechanisms

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### CNS

- Changes are significant, yet idiosyncratic
  - Decrease in weight and volume of brain
  - Alterations in cognition
- Increased sensitivity to medications
  - Benzodiazepines, opioids, anticholinergics, NSAIDs

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### CNS

- Cholinergic blockade
  - Sedation, confusion, and reduced ability to recall
    - TCAs, diphenhydramine, antispasmodics, antipsychotics
- Benzodiazepines can cause severe CNS depression
  - Leads to falls and hip fractures
  - Use caution and small dosages

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### Cardiovascular

- Decreased baroreceptor responsiveness
  - Results in orthostatic hypotension
    - Antihypertensives

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### GU

- Urinary incontinence
  - 15 to 30% of community-dwellers
  - 50% of nursing home residents
  - Enlarged prostate, urine retention

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### RISK FACTORS FOR ADEs

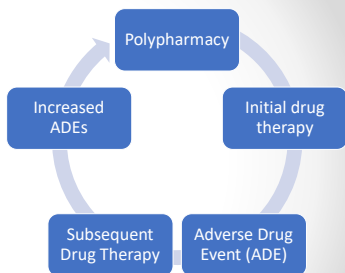
- 6 or more concurrent chronic conditions
- 12 or more doses of drugs / day
- 9 or more medications
- Prior adverse drug reaction
- Low body weight or body mass index
- Age 85 or older
- Estimated CrCl < 50 mL / min

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## Prescribing Cascades

- First reported in 1995
- Definition: An adverse drug event misinterpreted as a new medical condition resulting in a new medication being prescribed to treat the ADE.
- People of all ages can be affected



Trenaman, S.C., Bowles, S.K., Kirkland, S. et al. An examination of three prescribing cascades in a cohort of older adults with dementia. *BMC Geriatr* 21, 297 (2021).

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## Examples of prescribing cascades

Initial drug therapy	Adverse drug event	Subsequent drug therapy
Antipsychotics	Extrapyramidal signs and symptoms	Antiparkinsonian therapy
Cholinesterase inhibitors	Urinary incontinence	Incontinence treatment
Thiazide diuretics	Hyperuricemia	Gout treatment
NSAIDs	Increased blood pressure	Antihypertensive therapy

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## Successful Drug Therapy

- Uses the correct drug appropriately
- Prescribes the correct dosage
- Targets the correct condition
- Is appropriate for the patient
- Considers goals of care
- **Failure in any one of these can result in adverse drug events (ADEs)**

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Which of the following principles should NOT be followed when prescribing new medication(s) for an older adult?

- Start with a low dose
- Start all new medications simultaneously
- Titrate the dosage upward slowly
- Use one drug to treat two different conditions, if possible

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## Steps to Reduce Polypharmacy

1. Have patients keep an accurate record of all medications, including OTCs, herbals, and other alternative medicines
2. Identify drugs by generic name and drug class
3. Be aware of the prescribing cascade
4. Encourage patients to use one pharmacy and one primary care provider
5. Consider deprescribing when medications are potentially inappropriate or unnecessary

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## Comprehensive Medication Reconciliation and Review

1. Medication adherence
2. Therapeutic duplication
3. Drug interactions
4. Drug-Disease contraindications
5. Potentially inappropriate medication in older adults (e.g., Beers' criteria)
  - a. Pharmacokinetics of aging (Absorption, distribution, metabolism, and elimination)
  - b. Pharmacodynamics of aging
6. Chronic disease state management in older adults

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### Assess each medication, and ask

- What are the goals of care?
- Is this medication necessary?
- What are the therapeutic end points?
- Do the benefits outweigh the risks?
- Is it used to treat effects of another drug?
- Could 1 drug be used to treat 2 conditions?
- Could it interact with diseases, other drugs?
- Does patient know what it's for, how to take it, and what ADEs to look for?

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### Role of culture on medication use

- The role of family
- Sex-related norms
- Role of religion, spirituality, related rituals
- Media choices/Health literacy
- Use of indigenous healing practices
- Use of Western medicine
- How patients infer the meaning of their illness, death, and dying
- Advanced directives
- End-of-life care/Hospice Care/Symptom management

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### Role of social determinants of health on medication use

Nonmedical factors that impact health outcomes

- Conditions in which people are born, live, learn, work, play, worship and age
- ADLs/IADLs

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### Assessment of Risks and Benefits

#### HFrEF regimen

- Renal dysfunction,
- Low blood pressures
- Urinary incontinence

#### Anticoagulation

- Fall/bleed risk

#### Chronic opioid therapy

- Falls
- Cognitive impairment
- Constipation

#### Intensively treated diabetes

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### American Diabetes Association Standards of Care in Older Adults-2023

- **13.1** Consider the assessment of medical, psychological, functional (self-management abilities), and social domains in older adults to provide a framework to determine targets and therapeutic approaches for diabetes management. **B**
- **13.2** Screen for geriatric syndromes (i.e., polypharmacy, cognitive impairment, depression, urinary incontinence, falls, persistent pain, and frailty) in older adults, as they may affect diabetes self-management and diminish quality of life.
- **13.4** Because older adults with diabetes have a greater risk of hypoglycemia than younger adults, episodes of hypoglycemia should be ascertained and addressed at routine visits.
- **13.6** For older adults with type 2 diabetes on multiple daily doses of insulin, continuous glucose monitoring should be considered to improve glycemc outcomes and decrease glucose variability.

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### American Diabetes Association Standards of Care in Older Adults-2023

- **13.8** Older adults who are otherwise healthy with few coexisting chronic illnesses and intact cognitive function and functional status should have lower glycemc goals (such as A1C <7.0–7.5% [53–58 mmol/mol]), while those with multiple coexisting chronic illnesses, cognitive impairment, or functional dependence should have less-stringent glycemc goals (such as A1C <8.0% [64 mmol/mol]).
- **13.11** Treatment of hypertension to individualized target levels is indicated in most older adults.
- **13.12** Treatment of other cardiovascular risk factors should be individualized in older adults considering the time frame of benefit. Lipid-lowering therapy and aspirin therapy may benefit those with life expectancies at least equal to the time frame of primary prevention or secondary intervention trials.

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## Framework for Treatment Older Adults with Diabetes

Health status	Rationale	Reasonable A1C goal	Fasting or preprandial glucose	Bedtime glucose	Blood pressure
Healthy	Longer life-expectancy	<7.0–7.5%	80–130 mg/dL	80–180 mg/dL	<130/80 mmHg
Complex	Hypoglycemia/ Fall Risk	<8.0%	90–150 mg/dL	100–180 mg/dL	<130/80 mmHg
Very complex	Limited life-expectancy	Avoid reliance on A1C	100–180 mg/dL	110–200 mg/dL	<140/90 mmHg

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## Beers' criteria: Potentially Inappropriate Medication Use in Older Adults

1. Medications or classes to avoid in older adults
2. Diseases/conditions and medications to avoid in older adults with these diseases
3. Medications to be used with caution

2023 Beers' criteria. J Am Geriatr Soc. May 2023.

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## Inappropriate Medication Use in Older Adults (Beers' Criteria)

- 2023 Beers' criteria. Released in May 2023.
- 2019 Beers' criteria. J Am Geriatr Soc 00:1–21, 2019.
- 2015 Beers' criteria. J Am Geriatr Soc 2015.
- 2012 Beers' criteria. J Am Geriatr Soc 2012 60:616–31.
- Fick DM, et al. Arch Intern Med 2003;163:2716–2724.
- Medications or classes to avoid in older adults
- Diseases/conditions and medications to avoid in older adults with these diseases

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## Beers' Criteria: Independent of Diagnosis Analgesics

- Meperidine (long  $t_{1/2}$  metabolite, CNS)-Avoid
- Non-COX-selective NSAIDs, oral
  - Indomethacin (CNS)-Avoid
  - Ketorolac- (GI bleeds)-Avoid
  - Avoid chronic use of all others unless alternatives are not effective and patient can take gastroprotective agent
    - Aspirin >325 mg/day
- Skeletal muscle relaxants\*
  - (? Effectiveness/anticholinergic SE)-Avoid

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## Beers' Criteria: Independent of Diagnosis Psychiatric/CNS

- Antidepressants
  - Amitriptyline, doxepin >6 mg/day, clomipramine, nortriptyline, paroxetine(anticholinergic, orthostasis)
- Hypnotics/Anxiolytics
  - Benzodiazepines (↑ CNS/falls/MVAs, ↓ metabolism)
    - Short, intermediate, and long-acting
    - Long-acting may be appropriate for seizures/REM sleep\*
  - Nonbenzodiazepine hypnotics
    - Ezopiclone, zolpidem, zaleplon (CNS, falls, min. improvement sleep latency/duration, MVAs)
- Antipsychotics
  - All 1<sup>st</sup> and 2<sup>nd</sup> generation antipsychotics-Avoid
  - (↑ stroke, cognitive decline, mortality in dementia)
  - Except in schizophrenia, bipolar, and short-term use with chemotherapy

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## Beers' Criteria: Independent of Diagnosis Cardiovascular

- Alpha blockers for hypertension (orthostasis)
  - Doxazosin, prazosin, terazosin
- Alpha agonists, central (CNS/bradycardia/orthostasis)
  - Clonidine
- Amiodarone (greater toxicities)
  - Avoid 1<sup>st</sup>-line a. fib unless has heart failure
- Dronedarone (worse outcomes)
  - Avoid permanent a. fib/severe heart failure (HF/EF)
- Digoxin- avoid 1<sup>st</sup>-line a. fib/heart failure
- Dipyridamole, oral short-acting (orthostasis)\*
- Nifedipine IR (hypotension, ↑ MI)\*
- Rivaroxaban-long-term for a. fib/VTE (↑ major/GI bleed)\*
- Warfarin-a. fib/VTE (compared w/DOACs, ↑ major/GI bleed)\*
- Aspirin for primary prevention\*

\*Moved/added to "Avoid" in 2023 criteria

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### Beers' Criteria: Independent of Diagnosis Endocrine and GI

- Sulfonylureas, long-duration (hypoglycemia/SIADH)
  - Glyburide, glimepiride
- Insulin, sliding scale
- Megestrol (↑ thrombotic events)
- Growth hormone
- Estrogen-oral and topical patch
  - (↑ breast/endometrium cancer/clots, lack cardio or cognitive protection)
- Androgens: testosterone (cardiac)
- Desiccated thyroid (cardiac effects)
- Metoclopramide (EPS) (not to exceed 12 weeks)
- Mineral oil, oral (aspiration)
- Proton pump inhibitors (C. difficile/bone loss/bone fractures)
  - Avoid use >8 weeks, unless high-risk patients

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### Beers' Criteria: Independent of Diagnosis anticholinergics and anti-infective

- 1<sup>st</sup>-generation Antihistamines (anticholinergic)
  - Diphenhydramine, oral (confusion/sedation)
  - Chlorpheniramine
  - Meclizine
  - Promethazine
  - Hydroxyzine
- Antiparkinson agents
  - Benzotropine, trihexyphenidyl
- Antispasmodics-Avoid, except palliative care
  - Dicyclomine, hyoscyamine, scopolamine
- Nitrofurantoin
  - Avoid long-term suppression and CrCl<30 mL/min

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### Beers Criteria Considering Diagnosis

- Symptomatic heart failure: NSAIDs/COX-2 inhibitors, TZDs
  - diltiazem/ verapamil (avoid reduced EF)
- Syncope: AChEIs, non-selective alpha blockers, tertiary TCAs
- Delirium: TCAs, anticholinergics, benzos, H2RA, nonbenzos
- Dementia: anticholinergics, benzodiazepine, antipsychotics,
- Falls/Fractures: Anticonvulsants, antipsych, benzos, nonbenzo hypnotics, opioids, TCAs, SSRIs, SNRIs
- Parkinson disease:
  - All antipsychotics (except quetiapine, clozapine, pimavanserin)
  - Antiemetics: metoclopramide, prochlorperazine, promethazine

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### Beers Criteria Considering Diagnosis

- Gastric/duodenal ulcers: non-COX-2 selective NSAIDs and aspirin >325 mg
- CKD (stage IV/V): NSAIDs
- Urinary incontinence in women
  - All types: estrogen (oral and transdermal)
  - Stress/mixed: alpha blockers
- BPH: strong oral anticholinergics (except for UI)

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### To be used with caution

- Aspirin for primary prevention, age ≥ 70 years\*
- Dabigatran, age ≥ 75 years and CrCl < 30 mL/min\*
- Rivaroxaban-increased risk of serious bleeds compared to other anticoagulants\*
- May cause SIADH/hyponatremia
  - Antipsychotics
  - Diuretics
  - SSRIs, SNRIs, TCAs, Mirtazapine
  - Tramadol
- Dextromethorphan/quinidine (Nuedexta™)
  - ? Effectiveness in dementia
- Trimethoprim/Sulfamethoxazole (Bactrim™)
  - Increased hyperkalemia in combo with ACEI/ARBs in patients with CKD
- Sodium glucose co-transporter-2 inhibitors (SGLT2)\*\*
  - Increased risk urogenital infections

\*Moved to "Avoid" category in 2023 criteria

\*\*Added in 2023 criteria

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### Potentially Important Drug-Drug Interactions

- Refer to table 5 for full list
- Opioids-benzodiazepines-increased risk overdose
- Opioids-gabapentin/pregabalin-Increased risk overdose
- Phenytoin-Bactrim-Increase risk phenytoin toxicity
- Theophylline-Ciprofloxacin-Increase risk theophylline toxicity
- Warfarin-Increased risk of bleeding
  - Ciprofloxacin
  - Macrolides (excluding azithromycin)
  - Bactrim

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### Potentially Important Drug-Drug Interactions

- Multiple anticholinergics
- Increased risk of falls:
  - Benzodiazepines
  - Antidepressants (SSRIs/TCAs)
  - Antipsychotics
  - Opioids
- Corticosteroids/NSAIDs
- Peripheral alpha-blockers/loop diuretics
  - Increase risk urinary incontinence in older women
- Warfarin/NSAIDs

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### To be avoided or have their dosage reduced with varying levels of kidney function

- Refer to table 6 for full list
- Colchicine (CrCl <30) reduce dose
- Gabapentin (CrCl <60) reduce dose
- Enoxaparin (CrCl <30) reduce dose
- Rivaroxaban (CrCl 30) reduce dose
- Spironolactone (CrCl <30) Avoid
- Triamterene (CrCl <30) Avoid
- Ciprofloxacin (CrCl<30)-Increased risk CNS effects
- Bactrim (CrCl<30)-Worsening renal function and hyperkalemia

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### Inappropriate Drug Therapy based on Beers' Criteria

Authors	Setting	Prevalence of Inappropriate Prescribing
Goulding MR 2004	Ambulatory care visits	7.8% of visits
Zhan et al. 2001	Community dwelling elderly	21.3% of patients
Simon SR, et al. 2005	Elderly in managed care	28.8% of patients
Golden et al. 1999	Nursing home-eligible	39.7% of patients
NM Medicare Advantage plans 2009	New Mexico Medicare	21.5% of patients
Morin L, et al. 2016	Nursing homes North America	26.8% of patients

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### STOPP and START Criteria, Version 2

- Screening Tool of Older Persons' Prescriptions (STOPP)
  - Screening Tool to Alert doctors to Right Treatment (START)
- O'Mahony D, O' Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing. 2015;44(2):213-8.

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### Case: AB 81 year-old female with Medicare insurance

#### Problem List

1. CVA X 6
2. Osteoarthritis
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4. Diabetes, type 2
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7. Hypertension
8. Hypothyroidism
9. Hypercholesterolemia
10. Osteopenia
11. Urinary incontinence
12. Atrophic vaginitis
13. COPD
14. Frequent falls

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### AB's Medications

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## AB's Medications (continued)

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- Cl 104
- BUN 25
- Scr 1.3

- HbA1c 6.8%

- Mean blood glucose 164.8

- TSH 5.680

### •Lipids

- TC 144
- TG 258
- HDL 39
- LDL 53

- PE: Bilateral LE edema

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## Conclusions

- Age alters pharmacokinetics (drug absorption, distribution, metabolism, and elimination)
- Age alters pharmacodynamics
- ADEs are common among older patients
- Successful drug therapy means:
  - Choosing the correct dosage of the correct drug for the condition and individual patient
  - Monitoring the therapy
- Consider deprescribing when medications are potentially inappropriate or unnecessary

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