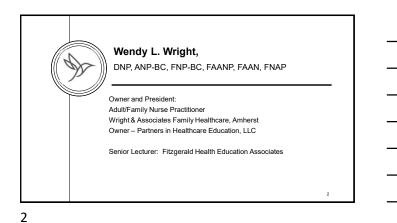
Safe Prescribing in the Older Adult

Presented by: Wendy L. Wright, DNP, ANP-BC, FNP-BC, FAANP, FAAN, FNAP

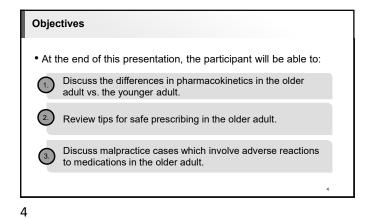
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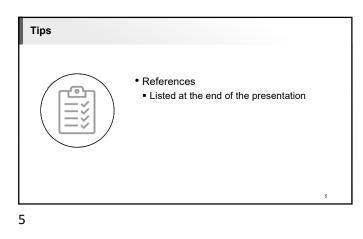


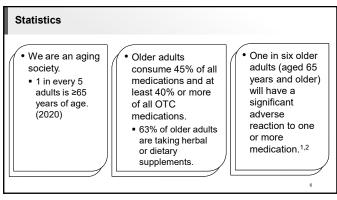
Disclosures

- Speaker Bureau
- Sanofi-Pasteur, Merck, Pfizer, Moderna, and Seqirus- Vaccines
- AbbVie and Biohaven Migraines
- Idorsia Insomnia
- Exact Sciences: Colorectal Cancer
- AstraZeneca: Asthma and COPD
- Consultant
- Sanofi-Pasteur, Merck, Pfizer, Moderna, and Seqirus Vaccines
 Idorsia Insomnia
- Shield Therapeutics Iron Deficiency Anemia

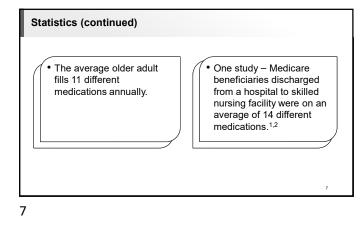
All relevant financial relationships have been mitigated











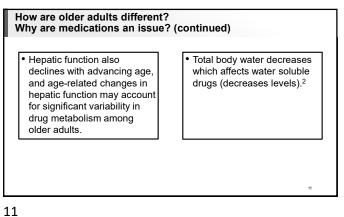
Prescribing in the Older Adult

- Requires special considerations because...
- Many drug trials do not include older adults.
- Older adults often have significant medical comorbidities which exclude them from clinical trials.
- Older adults are often on multiple medications, including OTC supplementation.
- Older adults often have age-related changes in pharmacokinetics (i.e., absorption, distribution, metabolism, and excretion).
- Older adults often have age-related changes in the pharmacodynamics of a medication (the physiologic effects of the drug).²

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 Pharmacokinetics What the body does to the drug This does change with age for a variety of reasons such as absorption, distribution, and excretion.

How are older adults different? Why are medications an issue?			
• The older adult may experience an increased volume of drug distribution due to an increase in body fat relative to skeletal muscle with aging.	• Drug clearance may be decreased due to the natural decline in renal function with age, even in the absence of renal disease.	• Larger drug storage reservoirs and decreased clearance prolong drug half-lives and lead to increased plasma drug concentrations in older people. ²	
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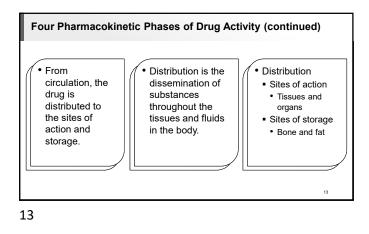
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Four Pharmacokinetic Phases of Drug Activity

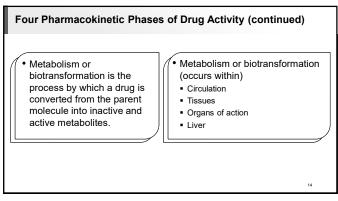
- Absorption The process of getting a drug into circulation
- Depending upon the drug and route of administration, absorption occurs in...
- Gastrointestinal tract
- Mucous membranes
- Muscle
- Skin
- Subcutaneous tissue

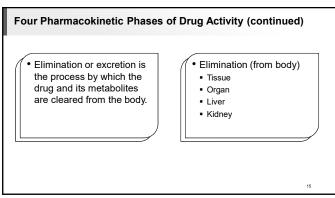
• Once absorbed, the drug is sent circulation.

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Factors Affecting Ab	sorption in the Older Adult
 Absorption Increased gastric pH (less acidic than middle-aged adult) Decreased GI motility in the older adult Decreased blood flow in the GI tract 	 In general, absorption of medications in the elderly is not significantly different from the younger adult except when Older adult is taking medications which affect gastric pH (PPI) Higher pH means less drug is broken down endering more available to be absorbed. Adult is taking drugs which alter motility or has a gastric emptying issue

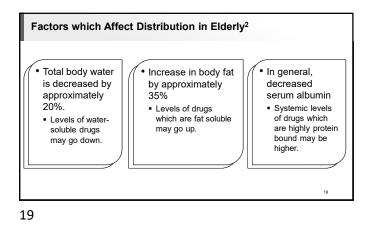
Examples of Medication Issues Related to Absorption²

- Proton pump inhibitors
- Decreased absorption of vitamin B₁₂, iron, calcium, and magnesium
- $\mbox{ }$ Increased risk of B_{12} deficiency, iron, and magnesium deficiencies
- Increased risk of osteoporosis and fractures
- Increased risk of CAP and C. difficile
- May increase risk of acute and chronic kidney disease

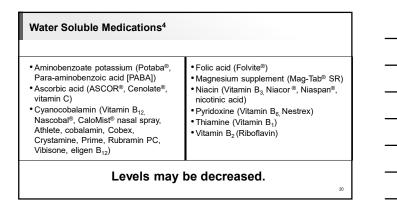
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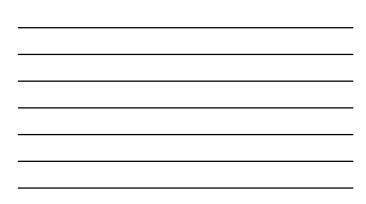
Medications which Impact Absorption ³			
 GLP-1 receptor agonists Exenatide Liraglutide Semaglutide Lixisenatide 	 Mechanism of action – Delay gastric emptying GLP-1RAs may produce clinically significant interactions with drugs that require achievement of target peak concentrations or a rapid onset of action. For instance, the area under curves (AUCs) of acetaminophen and lovastatin were decreased after exenatide administration and those of lisinopril and digoxin were decreased after liraglutide administration. 		
	18		







	Drug Name	Indication	Solubility In Water	Bioavailability
	Astemizole	Allergic Rhinitis	Insoluble	Low - moderate
	Cyclandelate	Peripheral vascular disease	Insoluble	Low
Eat Calubla	Perphenazine	Psychotic disorder	Insoluble	Low
Fat Soluble	Testosterone	Androgen Replacement Therapy	Insoluble	Low
	Famotidine	GERD	Slightly soluble	Low (39-50%)
Medications	Budesonide	Allergic Rhinitis	Sparingly soluble	Low (~15%)
Medications	Mesalamine	Irritable Bowel Syndrome	Slightly soluble	Low (~20%)
	Clemastine	Allergic Rhinitis	Slightly soluble	Low (~39%)
	Buprenorphine	Pain	Slightly soluble	Low (<30%)
	Sertraine	Anxiety	Slightly soluble	Low (\$44%)
	Auranofin	Arthritis	Slightly soluble	Low (15-25%)
	Felodipine	Hypertension	Insoluble	Low (15%)
	Isradipine	Hypertension	Insoluble	Low (15-24%)
	Danazol	Endometriosis	Insoluble	Low
Levels may be higher.	Loratadine	Allergic Rhinitis	Insoluble	Low
Levels may be might.	Isosorbide dinitrate	Angina	Sparingly soluble	Low (20-35%)
	Fluphenazine	Psychotic disorder	Insoluble	Low (2-3%)
	Spironolactone	Hypertension, Edema	Insoluble	Low (25%)
	Biperiden	Parkinson's disease	Sparingly soluble	Low (29-33%)
	Cyclosporin	Transplantation	Slightly soluble	Low (30%)
	Norfloxacin	Bacterial Infection	Slightly soluble	Low (30-40%)
	Cisapride	GERD	Insoluble	Low (35-40%)
	Nabumetone	Arthritis	Insoluble	Low (35%)
	Dronabinol	Antiemetic	Insoluble	Low 10-20%)
	Lovastatin	Hyperlipidemia		Low (~5%)
	Simvastatin	Hyperlipidemia	Insoluble	Low (<5%)



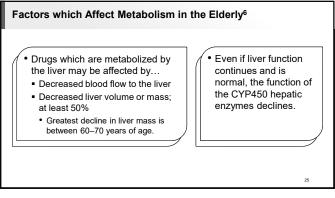
Examples of Highly Protein-bound Drugs			
Lower binding of these medications leads to higher systemic levels. (Increased risk of adverse events)			
 Amitriptyline Digoxin Furosemide Hydralazine Nortriptyline 	• Phenytoin • Propranolol • Spironolactone • Warfarin		
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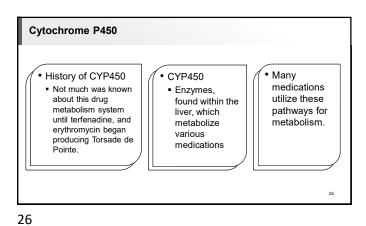
Additional Important Medications Affected by Distribution ⁵
 Diazepam – Volume of distribution is increased. Increased CNS depression Increase in respiratory depression Doses used in a younger person are going to increase risk of sedation, falls, and respiratory depression.
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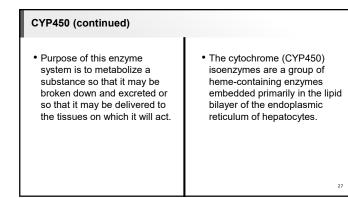
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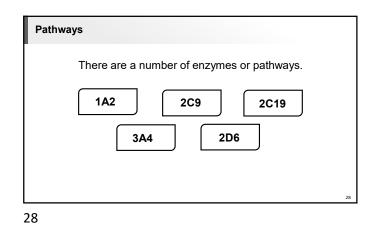
Beers Criteria⁵

- Benzodiazepines
- Short- and intermediate-acting
- Alprazolam, lorazepam, oxazepam, temazepam, triazolam
- Long-acting
- Clorazepate, chlordiazepoxide, chlordiazepoxide-amitriptyline, aclidiniumchlordiazepoxide, clonazepam, diazepam, flurazepam, and quazepam
- Older adults have increased sensitivity to benzodiazepines and slower metabolism of long-acting agents.
- In general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults.

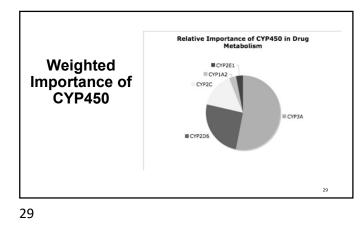




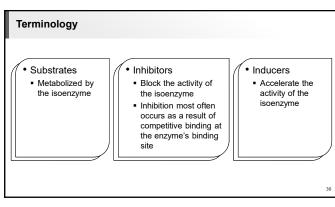






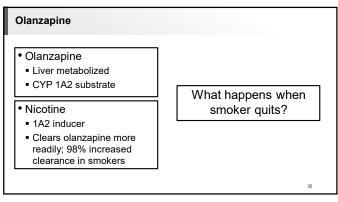


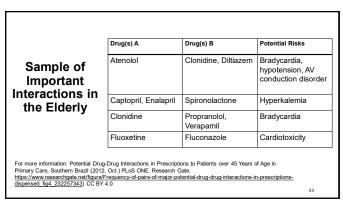




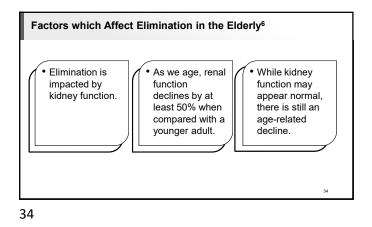
li	nhibitors are ranked.	
 Strong inhibitors >5-fold increase in the plasma AUC values or more than 80% decrease in clearance 	Moderate inhibitors >2-fold increase in the plasma AUC values or 50–80% decrease in clearance	• Weak inhibitors • >1.25-fold but <2-fold increase in the plasma AUC values or 20–50% decrease in clearance
L]	L	













Creatinine Clearance⁶ Creatinine – Inaccurate number GFR - Also, a very accurate number • Creatinine clearance - Much more accurate Many medications have moved to To adjust dosage to compensate for decreased GFR and away kidney function, creatinine clearance is one of from creatinine the most reliable formulas. clearance. Ideal creatinine clearance is 100–120 mL/min. • i.e., Metformin Download for healthcare professionals – Free online medical reference (MDcalc [app]); also available in mobile health app (Epocrates®)

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Metformin Updates⁸

- Metformin is contraindicated in patients with an eGFR below 30 mL/min/1.73 m².
- Starting metformin in patients with an eGFR between 30 to 45 mL/min/1.73 m² is not recommended.
- In patients taking metformin whose eGFR later falls below 45 mL/min/1.73 m², assess the benefits and risks of continuing treatment.
- Discontinue metformin at the time of or before an iodinated contrast imaging procedure in patients with an eGFR between 30–60 mL/min/1.73 m²; in patients with a history of liver disease, alcoholism, or heart failure; or in patients who will be administered intra-arterial iodinated contrast.
- GFR: 30-35 mL/min/1.73 m² Maximum dosage 1000 mg daily

Important Medications Affected By Clearance

Lithium

- Exclusively renally cleared
- Increased serum concentrations
- Narrow therapeutic index

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Patient Scenario

- 72-year-old female with bipolar disorder
- Treated with lithium 300 mg once daily (managed by psych NP)
 Has been on for years
- Lithium level 1.0 (last evaluated approximately 1-month ago)
- Diagnosed with hypertension by primary care provider and treated with hydrochlorothiazide

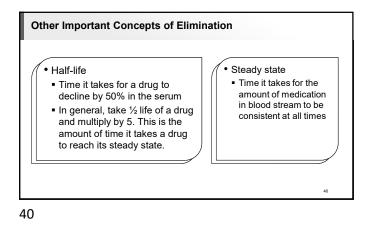
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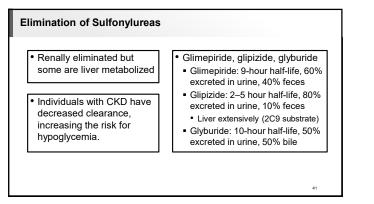
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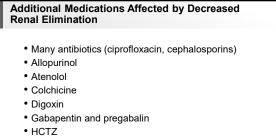
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Patient Scenario (continued)

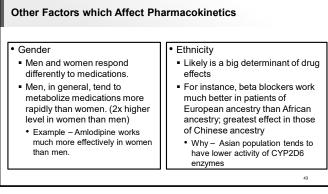
- 1-month later
- Tremulous, nauseated, confused
- Lithium level 2.6
- What happened?
- Can this occur with other medications?

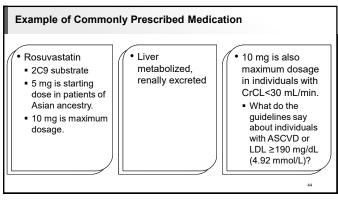




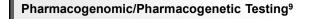


• Theophylline





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• What is it?

- Study of how a person's genes affect their metabolism of medications
- Numerous companies provide this service
- Covered by CMS (co-insurance) for most patients
- Can be really helpful in choosing medications or fine-tuning therapy

Beers Criteria

- First developed in 1991; most recent revision was 2019.
- Now includes more than 50 medications

Three categories
Medications to avoid

 Potentially inappropriate in those with certain conditions or syndromes

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Those to use with caution

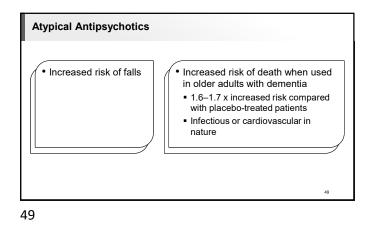
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Important Medication Classes to A Older Adults	Avoid Per Beers Criteria in
 Anticholinergic medications 1st generation antihistamines, antipsychotics, overactive bladder medications, tricyclic antidepressants, hyoscyamine, paroxetine Increased risk of cognitive decline and dementia (risk declines with medication discontinuation) 	 Anti-Parkinson agents Benztropine (oral) and trihexyphenidyl CNS depressants Increased effects

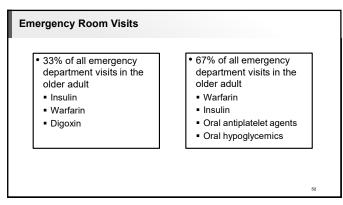
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Important Medication Classes to Avoid Per Beers Criteria in Older Adults (continued)

- Tertiary TCAs, alone or in combination
- Amitriptyline
- Chlordiazepoxide-amitriptyline
- Clomipramine
- Doxepin >6 mg/d
- Imipramine, perphenazine-amitriptyline







Warfarin (Coumadin®)

- First identified in the 1940s
- Became prominent in 1955 when Dwight D. Eisenhower was given warfarin after he suffered an MI.

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- At present, 2 million individuals are taking warfarin (Coumadin[®]).
- Yet only 1/3–1/2 of eligible patients are currently prescribed this drug.

Actions of Warfarin

- Inhibits the synthesis of vitamin K-dependent clotting factors which include – Factors II, VII, IX, and X; and the anticoagulant proteins C and S
- Completely absorbed after oral administration
- Peak concentration is attained within the first 4 hours.
- 98% of warfarin is bound to plasma proteins.
- Therefore, need to be aware that any highly protein bound drug added on to the individual taking warfarin may end up displacing warfarin (increasing warfarin levels and thus raising INR).

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GP

- GP failed to convert to NSR despite elective cardioversion.
- Opted to maintain her on warfarin
- 6 months into therapy
- INR which was previously controlled at 2.5–3.0
- Average 2.8
- Now INR 4.3
- What has changed?

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Review of Diet and Medication	s
 GP decided to start herself of cardiovascular disease prop Also wanted to improve her Numerous herbs can affect 	hylaxis. memory

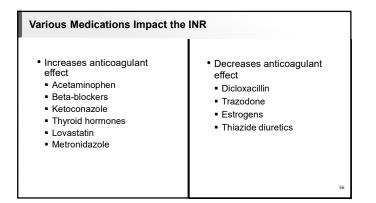
Drug Interactions

- Drug interactions involving warfarin are characterized as either pharmacokinetic or pharmacodynamic in nature.
 - Pharmacokinetic interactions cause changes in systemic concentrations of warfarin by interfering with 1 or more of the following...

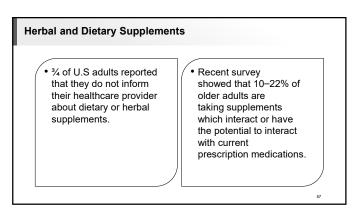
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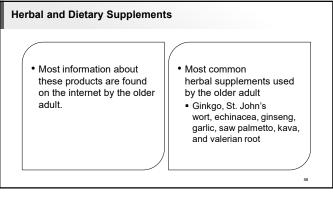
• Absorption, protein binding, metabolism

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Herbal Agents	Interacting Drugs	Clinical Effect
Danshen, Dong quai, Ginkgo biloba	Warfarin	Bleeding
Garlic, Ginseng,	Warfarin	Lowers blood level
St John's wort	Antidepressants, Cyclosporine, Digoxin	Serotonergic stimulation decreased cyclosporine effect, decreased serum digoxin level
Ginkgo biloba	Trazodone, morphine	Coma, lack of morphine effect
Kava	Benzodiazepines	CNS depression
Valerian	Anxiolytics	CNS sedation

RK1

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Malpractice Case	
 68-year-old male with diabetes and atrial fibrillation presents to a specialty NP for management of diabetes and high triglycerides. A1C - 8.2% (0.082 proportion), triglycerides - 1104 mg/dL (12.5 m Medications - Basal insulin, rapid acting insulin, atorvastatin, warfater - Multiple mechanisms of metabolism (CYP1A2 substrate, CYP2C substrate, CYP2C9 substrate, CYP3A4 substrate) 	arin
	60

Slide 59

- **RK0** Wendy to get permission to use, please see: https://www.ebmedicine.net/contact.php Renee Kirshner, 2022-09-12T23:26:53.642
- **RK1** Molly, if Wendy is able to get permission, I will add this in the back as part of the image source figures. Thanks Renee Kirshner, 2022-09-12T23:29:02.095
- MS1 0 I re-did this slide for the drug-drug interactions---Wendy will need to decide which program you want to keep these in Margaret Salinas, 2022-09-15T20:38:16.740

Malpractice Case (continued)

- INRs managed by primary care provider. Generally obtained monthly.
 Last INR 3 days ago and 2.1
- Fenofibrate added to regimen 48 mg once daily; told to follow-up with primary care provider for INR

Weak CYP2C9 inhibitor

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2 weeks later...

- Presents to emergency department
- Severe headache, confusion, abnormal neurological examination
- INR 9.2
- CT Confirms large subdural bleed, multiple locations
- Patient died over the next 72 hours.
- What happened and what could have been done differently?

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Polypharmacy in the Elderly

- Society is conditioned to believe that a pill fixes everything.
- Many clinicians are conditioned to believe that a pill is always needed.
- Finding the balance is always the key.
- Consequences
- Adverse events
- Drug-drug interactions
- Cost
- Decreased quality of life

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Adverse Drug Events (AEs)

- More than 2 million every year
- More than 100,000 deaths annually
- \bullet More than 95% are predictable and 50% preventable
- These increase significantly when an individual is on 5 or more medications.

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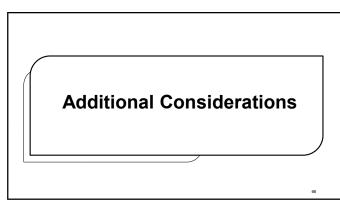
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Risks for AEs in the Older Adult⁶

- · Low body weight
- Age ≥85 years
- >12 or more medication doses per day
- 6 or more medications
- GFR <60 mL/min/1.73 m²

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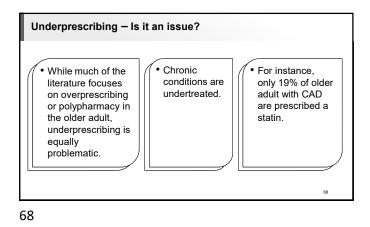


Macrolides

• Known QT prolongation

- Caution with other drugs which have similar potential...
- Tricyclic antidepressants
- Fluoroquinolones
- Antipsychotics
- Antiarrhythmics

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Common Time for Medication Confusion

- Discharge from hospital or long-term care facility
- Inappropriate medications or duplication of medications are common.
- \bullet 23% of older adults experience an adverse drug event after discontinued from hospital; 1/2 are preventable
- Transition of care visit is essential.

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Transition of Care Visit

- 72-year-old male
- Hypertension, gout, atrial fibrillation, hyperlipidemia, sleep apnea (treated with CPAP)
- Allergies Amlodipine (ankle edema), HCTZ (gout)
- Medications
- Allopurinol 300 mg daily, lisinopril 20 mg BID, flecainide daily, pravastatin

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Transition of Care Visit (continued) 72-year-old male (cont.) Admitted to hospital for angioedema and stridor after 15+ years on an ACE inhibitor Cardiology started patient on clonidine 0.1 mg TID. BP – 136/82 mm Hg at TIC visit; tolerating well and feeling well

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3 Months Later

- Patient's wife comes in for a visit with patient.
- He is restless and combative during night.
- Having terrible dreams, punched her in the head.
- She is scared for her safety during night and has begun to sleep in a different room.
- What is going on?

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Clonidine

- Other common adverse effects may include...
- Drowsiness, dizziness
- Feeling tired or irritable
- Cold symptoms, such as runny/stuffy nose, sneezing, cough, sore throat

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- Mood changes
- Sleep problems (insomnia), nightmares
- Headache, ear pain
- Mild fever
- Feeling hot

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Important Strategies for Prescribing in the Older Adult

- Print medication list for patient (brand and generic names).
- Ask patient to bring in medications with every visit (including supplements).
- Reconcile medications at every visit.
- Use a few drugs well rather than a lot of drugs poorly.
- Start low and go slow.
- Avoid multiple dosages each day.
- · Follow up when starting a new medications.
- Avoid medication cascade.

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I would be happy to entertain any questions you have!

End of Presentation! Thank you for your time, attention.

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