



Medication Use in the Elderly

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2018 presentation created by Katherine Fuller,
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Slides for 2019 updated by Jason Funaro,
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- Review pharmacokinetic changes in the elderly
- Discuss the 2019 Updated Beers Criteria for potentially inappropriate medication use in older adults
- Evaluate strategies to reduce adverse drug events in the elderly



- Up to 16.6% of all hospital admissions in elderly have been contributed to by adverse drug reactions (ADR)
 - Up to 88% of ADR related hospitalizations in elderly are preventable



- 65.7% of hospitalizations due to unintentional overdoses
- Four medications/drug classes contributed to 67% of hospitalizations:
 - Warfarin (Coumadin): 33.3%
 - Insulin: 13.9%
 - Oral antiplatelet medications: 13.3%
 - Aspirin, clopidogrel (Plavix), prasugrel (Effient), etc
 - Oral hypoglycemic agents: 10.7%
 - Glyburide (Diabeta), glimepiride (Amaryl), etc



ADE occurred following 18.7% of discharges

- Over 50% within 14 days of discharge

16.5% of ADEs due to Beers Criteria med

- Most common ADE meds: CV, diuretics, opioids, antibiotics, anticoagulant/antiplatelet agents

35% of ADEs were considered preventable

- 32% of the preventable ADEs were considered serious



What are common adverse drug events in geriatric patients?



Absorption

- Increased stomach pH; slowed gastric emptying

Distribution

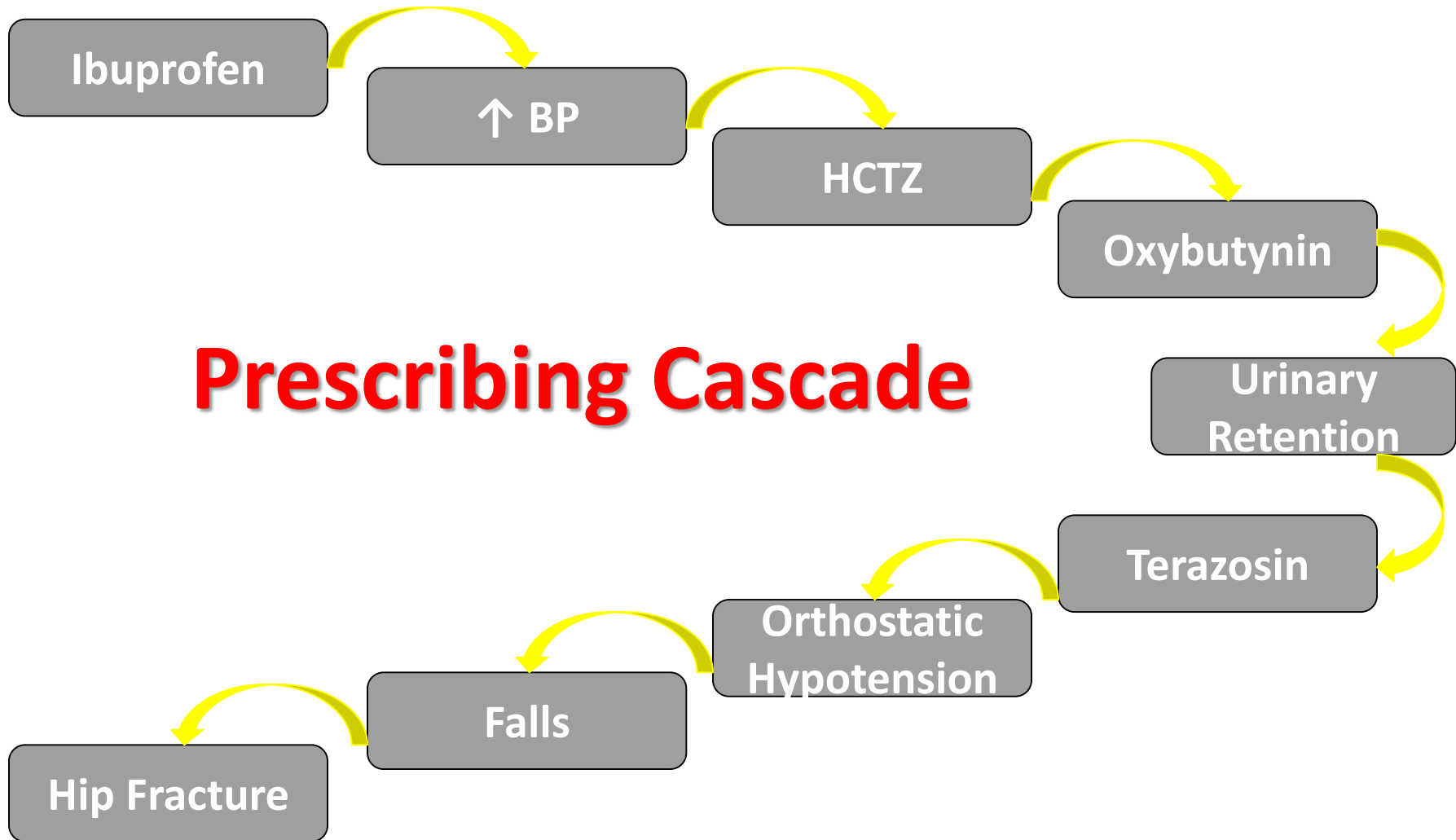
- ↓ muscle mass; ↑ adipose tissue; ↓ albumin

Metabolism

- ↓ Phase 1 P450 metabolism; no change for Phase 2 (conjugation reactions)

Elimination

- ↓ CrCl and ↓ GFR



Prescribing Cascade

Polypharmacy Causes



Patient Factors

- Multiple comorbidities (“A pill for every ill”)
- Non-adherence to current therapies

Prescriber Factors

- Inappropriate prescribing
- Lack of de-escalating therapies

System Factors

- Multiple pharmacies, multiple prescribers
- Direct-to-consumer advertising
- A culture that promotes “a pill for every ill”



- Adverse drug reactions
- Increased risk of drug-drug interactions
- Worsened health outcomes
- Excessive costs

Beers Criteria for Potentially Inappropriate Medication Use in Older Adults



Created in 1991 by the late geriatrician Mark Beers, MD

A list of high-risk medications that that should generally be avoided in older adults ≥ 65

Updated every ~3 years, available online at:

www.americangeriatrics.org

*Last published 2019



Guideline Goals

Improve medication selection

Educate clinicians and patients

Reduce adverse drug events

Serve as a tool for evaluating quality, cost, and patterns of care

Medication Inclusion Criteria

1. Potentially inappropriate in most older adults

2. Avoid in older adults with certain conditions

3. Use with caution in older adults

4. Significant drug-drug interactions

5. Need renal dose adjustment

Beers Criteria



Therapeutic Category/ Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Alpha ₁ blockers Doxazosin Prazosin Terazosin	High risk of orthostatic hypotension; not recommended as routine treatment for hypertension; alternative agents have superior risk/benefit profile.	Avoid use as an antihypertensive.	Moderate	Strong



Read this to understand why drug is considered potentially inappropriate in older adults, e.g., frequent adverse events, risk/benefit profile, other guideline recommendations.



Read this to understand in what circumstances the drug is considered a potentially inappropriate medication (PIM). In this example, use of an alpha₁-blocker for routine treatment of hypertension is considered potentially inappropriate. Use for other conditions such as lower urinary tract symptoms in men is **not** considered potentially inappropriate by this criterion. However, this does not automatically make the medication appropriate; usual clinical judgment applies.



Quality of evidence on which recommendation is based. Evidence was rated by the Beers panel based on a structured process.



Strength of recommendation. This was decided by the Beers panel based on the anticipated balance of risks and benefits from the medication.

1. Select Potentially Inappropriate Medications



Therapeutic Category	Select Agents in Class	Recommendation/ Rationale
Antidepressants	<u>Tricyclic Antidepressants (TCAs)</u> Amitriptyline (Elavil®) Nortriptyline (Pamelor®)	Avoid – highly anticholinergic and sedating
	<u>Others:</u> paroxetine (Paxil®)	
Antiemetics	Promethazine (Phenergan®) Meclizine (Antivert®)	Avoid – highly anticholinergic
Antihistamines (not all)	Diphenhydramine (Benadryl®) Hydroxyzine (Vistaril®) Chlorpheniramine (Aller-Chlor®)	Avoid – highly anticholinergic and sedating
Barbiturates	Butalbital (Fioricet®) Phenobarbital (Phenobarb®)	Avoid – high rate of physical dependence, greater risk of overdose
Benzodiazepines	Diazepam (Valium®) Alprazolam (Xanax®) Clonazepam (Klonopin®)	Avoid – increased sensitivity in older adults → falls, delirium

1. Select Potentially Inappropriate Medications



Therapeutic Category	Select Agents in Class	Recommendation/ Rationale
Cardiovascular Agents	Digoxin (Lanoxin [®])	Avoid in doses > 0.125 mg/day, not 1 st line for afib or heart failure
	<u>Alpha-1 Blockers</u> Doxazosin (Cardura [®]) Prazosin (Minipress [®])	Avoid – high risk of orthostatic hypotension
Anti-hyperglycemics	<u>Long-Acting Sulfonylureas (SUs)</u> Glyburide (Diabeta [®]) Glimepiride (Amaryl [®])	Avoid – high risk of severe prolonged hypoglycemia
	Insulin regimens using sliding scale only	Avoid - risk > benefit
Estrogens	Any systemic estrogen therapy	Avoid – risk of carcinogenic effect exceeds benefit
Hypnotics (“Z-drugs”)	Zolpidem (Ambien [®]) zaleplon (Sonata [®]), eszopiclone (Lunesta [®])	Avoid – similar ADE profile to that of benzos

1. Select Potentially Inappropriate Medications



Therapeutic Category	Select Agents in Class	Recommendation/ Rationale
NSAIDs	Indomethacin (Indocin [®]) Ketorolac (Toradol [®]) Chronic use of other NSAIDs	Avoid – risk of GI bleed
Skeletal Muscle Relaxants	Cyclobenzaprine (Flexeril [®]), carisoprodol (Soma [®]), methocarbamol (Robaxin [®])	Avoid – anticholinergic, limited efficacy
Dessicated Thyroid Products	Armour thyroid [®]	Avoid – safer alternatives available
Appetite Stimulants	Megestrol (Megace [®])	Avoid – risk of thrombotic events
Antiparkinsonian Agents	Benztropine (Cogentin [®]) Trihexylphenidyl	Avoid – don't use for EPS, more effective agents available
Proton Pump Inhibitors	Pantoprazole (Protonix [®]), esomeprazole (Nexium [®]), omeprazole (Prilosec [®]), etc.	Avoid scheduled use > 8 weeks, risk of C. diff, fractures

2. Select Drug-Disease / Drug-Syndrome Interactions

Syndrome/Disease	Agents to Avoid
Heart Failure	<ul style="list-style-type: none">• Certain calcium channel blockers (diltiazem, verapamil)• NSAIDs (use with caution, avoid if symptomatic)• Thiazolidinediones (pioglitazone, rosiglitazone)
Syncope	<ul style="list-style-type: none">• Acetylcholinesterase inhibitors (e.g. donepezil, rivastigmine)• Tricyclic antidepressants• Nonselective peripheral alpha-1 blockers (e.g. prazosin)• Certain antipsychotics (olanzapine, chlorpromazine)
Dementia or Cognitive Impairment	<ul style="list-style-type: none">• Anticholinergics• Benzodiazepines• Nonbenzodiazepine, benzo receptor agonists (e.g. zolpidem)• Antipsychotics
History of Falls/Fractures	<ul style="list-style-type: none">• Benzodiazepines & Z-drug hypnotics• Opioids• Antidepressants (TCAs, SSRIs, SNRIs)• Antiepileptics

3. Select Medications to Use with Caution in Older Adults



Agents	Risk in Older Adults
Trimethoprim-sulfamethoxazole (Bactrim, Septra)	<ul style="list-style-type: none">• Increased risk of hyperkalemia when used concurrently with ACE-I or ARB in presence of decreased creatinine clearance
Antipsychotics Carbamazepine/ oxcarbazepine Diuretics Mirtazapine SNRIs, SSRIs, TCAs Tramadol	<ul style="list-style-type: none">• May exacerbate or cause SIADH or hyponatremia• Monitor sodium levels closely on initiation or dose changes

4. Select Drug-Drug Interactions



Object Medication or Drug Class	Interacting Drug or Class	Rationale	Recommendation
RAS inhibitors (ACEIs, ARBs, aliskiren) or potassium-sparing diuretics (amiloride, triamterene)	Other RAS inhibitors	Hyperkalemia risk	Avoid routine use in patients with CKD stage ≥ 3
Anticholinergics	Anticholinergic	\uparrow Risk of cognitive decline	Avoid, minimize number of anticholinergics
Antidepressants Antipsychotics Antiepileptics Benzodiazepines Z-drugs Opioids	≥ 2 other CNS-active drugs	Fall and fracture risk	Minimize number of CNS-active drugs if possible
Corticosteroids	NSAIDs	Risk of ulcers	Avoid combination if possible or give GI protection

4. Select Drug-Drug Interactions



Object Medication or Drug Class	Interacting Drug or Class	Rationale	Recommendation
Peripheral alpha-1 blockers	Loop diuretics	↑ Urinary incontinence	Avoid in older women unless conditions warrant
Warfarin	Amiodarone NSAIDs Ciprofloxacin Macrolides (excluding azithromycin) Sulfamethoxazole-trimethoprim	↑ Bleeding risk	Avoid if possible; monitor INR closely

4. Select Drug-Drug Interactions



Object Medication or Drug Class	Interacting Drug or Class	Rationale	Recommendation
Opioids	Benzodiazepines	↑ overdose risk	Avoid
	Gabapentin, pregabalin	↑ severe sedation-related adverse events (e.g. respiratory depression, death)	Avoid, exceptions are made when transitioning from opioid therapy to gabapentinoid to reduce opioid dose

5. Select Renal Dose Adjustments



Medication	CrCl (mL/min)	Rationale	Recommendation
Amiloride	< 30	↑ K, ↓ Na	Avoid
Spiro lactone	< 30	↑ K	Avoid
Triamterene	< 30	↑ K, ↓ Na	Avoid
Duloxetine	< 30	↑ GI effects	Avoid
Gabapentin	< 60	CNS adverse effects	Reduce dose
Levetiracetam	≤ 80	CNS adverse effects	Reduce dose
Pregabalin	< 60	CNS adverse effects	Reduce dose

5. Select Renal Dose Adjustments



Medication	CrCl (mL/min)	Rationale	Recommendation
Tramadol	< 30	CNS adverse effects	IR: decrease dose ER: avoid
Cimetidine Famotidine Nizatidine Ranitidine	< 50	Mental status changes	Reduce dose
Colchicine	< 30	GI, neuromuscular, bone marrow toxicities	Reduce dose and closely monitor for adverse effects
Probenecid	< 30	Loss of efficacy	Avoid

5. Select Renal Dose Adjustments



Medication	CrCl (mL/min)	Rationale	Recommendation
Ciprofloxacin	< 30	Increased risk of seizures, tendon rupture, confusion	Avoid or dose reduce
Trimethoprim-sulfamethoxazole	< 30	↑ K, ↓ eGFR	Reduce dose if 15-29 mL/min, avoid if <15
Dofetilide (Tikosyn)	< 60	QTc prolongation, risk of torsades de pointes	



CARING FOR ELDERLY POPULATIONS



- High risk agents
- Assessment and monitoring
 - S/S of bleeding and/or thrombosis
 - Renal and/or hepatic changes
 - Drug interactions
 - Dietary considerations (warfarin)
 - Upcoming procedures
 - Duration of therapy



- Increase INR
 - “FAB-4”
 - Fluconazole
 - Amiodarone
 - Bactrim (sulfamethoxazole/trimethoprim)
 - Flagyl (metronidazole)
 - Consider proactively reducing warfarin for these agents
 - Ensure anticoagulation clinic follow-up
- Decrease INR
 - Rifampin, carbamazepine
- Maintain consistent dietary vitamin k intake
 - High vitamin k intake → decreased INR

This is not a comprehensive list!

Direct Oral Anticoagulants



- Agents:
 - Apixaban (Eliquis), rivaroxaban (Xarelto), dabigatran (Pradaxa), edoxaban (Savaysa)
 - Dabigatran and rivaroxaban: Use with caution in patients ≥ 75
 - Greater risk of GI bleeding vs. warfarin
- Duke Anticoagulation Fact Sheets
 - Available on the Duke Intranet Formweb site, under Medication Usage Guidelines:
 - <http://formweb.com/duke/>

Direct Oral Anticoagulants



Medication	Renal Dose Adjustment	Recommendation
Apixaban (Eliquis)	ESRD on dialysis	Dose reduction vs. not
	Afib with ≥ 2 of: SCr ≥ 1.5 , age ≥ 80 , wt < 60 kg	Reduce dose
Dabigatran (Pradaxa)	CrCl < 30 mL/min	Avoid
Edoxaban (Savaysa)	CrCl 15-50 mL/min	Reduce dose
	CrCl < 15 OR > 95 mL/min	Avoid
Rivaroxaban (Xarelto)	CrCl 30-50 mL/min	Decrease dose
	CrCl < 30 mL/min	Avoid

Monitoring: CBC, SCr, hepatic function panel



- Prasugrel (Effient ®): Use with caution in patients ≥ 75
 - Greater risk of bleeding
- Aspirin for **primary** prevention of cardiovascular disease in patients ≥ 70
 - The recently published ASPREE trial confirms there is a lack of evidence of benefit when compared to risks
 - Use with caution



- Aimed to evaluate the effect of aspirin on cardiovascular events and bleeding in **healthy elderly** (age \geq 65-70)
 - No coronary heart disease, cerebrovascular disease, atrial fibrillation, dementia, uncontrolled hypertension, high risk of bleed, or anemia
 - Patients on anticoagulation or with compelling indication for aspirin were excluded
- Randomized patients in a 1:1 ratio to aspirin 100 mg daily vs. placebo



- N=19,114 patients enrolled, 9,525 on aspirin and 9,589 on placebo
 - Median of 4.7 years of follow up

When used for primary prophylaxis in elderly patients, low dose aspirin:

1. Does not significantly reduce risk of CVD
2. Increases risk of GI & intracranial bleed

95% CI: 1.18 to 1.62, P<0.001)

- **Upper GI bleed:** HR 1.87 (95% CI: 1.32 to 2.66)
- **Intracranial bleed:** HR 1.5 (95% CI: 1.11 to 2.02)



- Anticholinergics
- Benzodiazepines
 - Increase risk for cognitive impairment, delirium, falls, fractures
 - Chronic uses have higher risk of cognitive decline
- Non-benzodiazepine hypnotics (“Z-drugs”)
 - Similar adverse effect profile to benzodiazepines
- H₂-receptor antagonists
- Anti-psychotics



Select Strong Anticholinergic Medications

Amitriptyline (Elavil)	Imipramine (Tofranil)
Benzotropine (Cogentin)	Meclizine (Antivert)
Brompheniramine (Dimetapp)	Nortriptyline (Pamelor)
Chlorpheniramine (Chlor-Trimeton)	Olanzapine (Zyprexa)
Clemastine (Tavist)	Orphenadrine (Norflex)
Clozapine (Clozaril)	Oxybutynin (Ditropan)
Cyclobenzaprine (Flexeril)	Paroxetine (Paxil)
Darifenacin (Enablex)	Prochlorperazine (Compazine)
Diphenhydramine (Benadryl)	Promethazine (Phenergan)
Doxepin (Sinequan) at doses > 6 mg	Scopolamine (Transderm-Scop)
Doxylamine (Unisom)	Solifenacin (Vesicare)
Fesoterodine (Toviaz)	Tolterodine (Detrol)
Hydroxyzine (Atarax, Vistaril)	Trospium (Sanctura)
Hyoscyamine (Levsin)	



Anticholinergics may increase the risk of cognitive impairment

- A 46% increase over 6 years has been shown

Anticholinergic medications have been associated with increased mortality at 2 years

- Dose-response effect

Anticholinergic Side Effects



Anti-SLUD: Salivation, Lacrimation, Urination, Defecation

ANTICHOLINERGIC SIDE EFFECTS



Hot as a hare



Dry as a bone



Blind as a bat



Red as a beet



Mad as a hatter

sketchymedicine.com

**“Hot as a hare, blind as a bat,
dry as a bone, red as a beet,
mad as a hatter”**

**“Can’t see, can’t pee,
Can’t spit, can’t...
...defecate”**

Medications that Increase Fall Risk



Effect	Medication
Hypotension	Tricyclic antidepressants (e.g. amitriptyline), antipsychotics, diuretics, erectile dysfunction medications Orthostatic hypotension: tamsulosin, trazodone, clonidine, carbidopa/levodopa
Sedation	Benzodiazepines, nonbenzodiazepine hypnotics (e.g. zaleplon, eszopiclone), antipsychotics, skeletal muscle relaxants, anticholinergic agents, opioids, anticonvulsants
Hypoglycemia	Insulin, oral hypoglycemic agents



- Opioids
- Anticholinergics (see prior slide)
- Tricyclic antidepressants:
 - (Amitriptyline (Elavil®), Nortriptyline (Pamelor®))
- Calcium channel blockers
 - E.g., verapamil (Calan ®)
- Antacids
 - Calcium carbonate (Tums)
- Iron products



- Target BP
 - <130/80 mmHg (per the 2017 AHA/ACC HTN guidelines)
- First line: CCB, thiazide diuretic, ACEI, ARB
 - Evaluate for compelling indications for one agent over another



- American Geriatrics Society and Choosing Wisely recommend:
 - Avoid using medications other than metformin to achieve $A1c < 7.5\%$ in most older adults
- ADA Goal Recommendations:

Consider A1c Goal < 8%:	Consider Goal < 8.5%:
<ul style="list-style-type: none">- Intermediate life expectancy- Falls or hypoglycemia risks, including 2+ ADL impairments- Mild to moderate cognitive impairment	<ul style="list-style-type: none">- Moderate-to-severe cognitive impairment- Very complex/poor health with limited life expectancy



- Avoid glyburide, glimepiride due to increased risk of prolonged hypoglycemia
 - Consider glipizide as an alternative
- Metformin dosing in renal impairment

eGFR Cutoff	Recommendation
> 45 mL/min/1.73m ²	No dose adjustment necessary
30-45 mL/min/1.73m ²	<ul style="list-style-type: none">• Do not initiate metformin• If already on metformin consider risk vs. benefit of continuing therapy• If continuing, dose reduce by 50%
< 30 mL/min/1.73m ²	Use is contraindicated



- Avoid first-generation antihistamines
 - Examples: diphenhydramine, chlorpheniramine, hydroxyzine
 - Use of diphenhydramine for acute treatment may be appropriate
 - e.g., severe allergic reactions
- Use loratadine (Claritin®), cetirizine (Zyrtec®), fexofenadine (Allegra®)



- Optimize treatment for contributing conditions
 - Depression, pain, etc.
- Sleep hygiene
- Cognitive behavioral therapy for insomnia
 - [Veteran's Affairs developed app: CBT-I Coach](#)
 - [www.cbtforinsomnia.com](#)
- Avoid sedative hypnotics, benzodiazepines, diphenhydramine, and amitriptyline



- Benzodiazepines
 - Increase risk for cognitive impairment and falls (as previously discussed)
- Non-BZD Hypnotics
 - Minimal improvement in sleep latency/duration
 - Similar adverse events to BZDs
 - Zolpidem in women: Limit IR to 5 mg and ER form to 6.25 mg



- Non-pharmacological options 1st line
- Pharmacologic considerations
 - Melatonin 3-5 mg daily
 - Doxepin 3-6 mg daily within 30 minutes prior to bedtime, do not exceed 6 mg/day



- Avoid benzodiazepines, if possible
- Consider counseling
 - e.g., [Silver Linings](#)
- Consider trial of SSRI, SNRI, or buspirone



- Non-pharmacologic
 - Heat and cold, physical therapy, and massage
- Pharmacologic
 - Avoid NSAIDs and skeletal muscle relaxants due to sedation risk and anticholinergic effects
 - Consider scheduled acetaminophen 1000 mg TID
 - Consider topical capsaicin or lidocaine
 - If opioids are required, ensure appropriate education
 - GI, CNS, falls, and respiratory risks



- Proton Pump Inhibitors are often overused and carry risks:
 - Increased risk of *C difficile* infections
 - Increased bone loss and fracture risk
 - B12 malabsorption (reasonable to periodically assess with long-term use)
- Avoid use > 8 weeks unless high-risk
 - Chronic NSAID use
 - Erosive esophagitis
 - Failure of discontinuation trial etc.



- Avoid promethazine, meclizine
- Avoid metoclopramide
 - May cause extrapyramidal effects, including tardive dyskinesia
 - Risk may be increased in frail elderly
 - Consider for gastroparesis if benefits > risks
- Consider ondansetron



MASTER

M = Minimize number of drugs used

A = Alternatives should be considered

S = Start low and go slow

T = Titrate therapy

E = Educate the patient and caregiver

R = Review regularly



Obstacles to Medication Management in Elderly

Childproof caps

Ability to correctly use nebulizer

Ability to correctly use inhalers

Ability to use blood glucose meter

Interpretation of medication labels

Difficulty recognizing color of pills

Large pill size



Medication Use in the Elderly

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